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Commission royale sur les nouvelles techniques de reproduction

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NEW REPRODUCTIVE
TECHNOLOGIES
AND THE SCIENCE,
INDUSTRY, EDUCATION,
AND SOCIAL WELFARE
SYSTEMS IN CANADA

Research Studies of the Royal Commission on New Reproductive Technologies



New
Reproductive
Technologies and
the Science, Industry,
Education, and
Social Welfare
Systems in
Canada

Volume 5 of the Research Studies

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Consistent with the Commission's commitment to full equality between men and women, care has been taken throughout this volume to use gender-neutral language wherever possible.



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Preface from the Chairperson



As Canadians living in the last decade of the twentieth century, we face unprecedented choices about procreation. Our responses to those choices — as individuals and as a society — say much about what we value and what our priorities are. Some technologies, such as those for assisted reproduction, are unlikely to become a common means of having a family — although the number of children born as a result of these techniques is greater than the number of infants placed for adoption in Canada. Others, such as ultrasound during pregnancy, are already generally accepted, and half of all pregnant women aged 35 and over undergo prenatal diagnostic procedures. Still other technologies, such as fetal tissue research, have little to do with reproduction as such, but may be of benefit to people suffering from diseases such as Parkinson's; they raise important ethical issues in the use and handling of reproductive tissues.

It is clear that opportunities for technological intervention raise issues that affect all of society; in addition, access to the technologies depends on the existence of public structures and policies to provide them. The values and priorities of society, as expressed through its institutions, laws, and funding arrangements, will affect individual options and choices.

As Canadians became more aware of these technologies throughout the 1980s, there was a growing awareness that there was an unacceptably large gap between the rapid pace of technological change and the policy development needed to guide decisions about whether and how to use such powerful technologies. There was also a realization of how little reliable information was available to make the needed policy decisions. In addition, many of the attitudes and assumptions underlying the way in which technologies were being developed and made available did not reflect the profound changes that have been transforming Canada in recent decades. Individual cases were being dealt with in isolation, and often in the absence of informed social consensus. At the same time, Canadians were looking

more critically at the role of science and technology in their lives in general, becoming more aware of their limited capacity to solve society's problems.

These concerns came together in the creation of the Royal Commission on New Reproductive Technologies. The Commission was established by the federal government in October 1989, with a wide-ranging and complex mandate. It is important to understand that the Commission was asked to consider the technologies' impact not only on society, but also on specific groups in society, particularly women and children. It was asked to consider not only the technologies' scientific and medical aspects, but also their ethical, legal, social, economic, and health implications. Its mandate was extensive, as it was directed to examine not only current developments in the area of new reproductive technologies, but also potential ones; not only techniques related to assisted conception, but also those of prenatal diagnosis; not only the condition of infertility, but also its causes and prevention; not only applications of technology, but also research, particularly embryo and fetal tissue research.

The appointment of a Royal Commission provided an opportunity to collect much-needed information, to foster public awareness and public debate, and to provide a principled framework for Canadian public policy on the use or restriction of these technologies.

The Commission set three broad goals for its work: to provide direction for public policy by making sound, practical, and principled recommendations; to leave a legacy of increased knowledge to benefit Canadian and international experience with new reproductive technologies; and to enhance public awareness and understanding of the issues surrounding new reproductive technologies to facilitate public participation in determining the future of the technologies and their place in Canadian society.

To fulfil these goals, the Commission held extensive public consultations, including private sessions for people with personal experiences of the technologies that they did not want to discuss in a public forum, and it developed an interdisciplinary research program to ensure that its recommendations would be informed by rigorous and wide-ranging research. In fact, the Commission published some of that research in advance of the Final Report to assist those working in the field of reproductive health and new reproductive technologies and to help inform the public.

The results of the research program are presented in these volumes. In all, the Commission developed and gathered an enormous body of information and analysis on which to base its recommendations, much of it available in Canada for the first time. This solid base of research findings helped to clarify the issues and produce practical and useful recommendations based on reliable data about the reality of the situation, not on speculation.

The Commission sought the involvement of the most qualified researchers to help develop its research projects. In total, more than 300

scholars and academics representing more than 70 disciplines — including the social sciences, humanities, medicine, genetics, life sciences, law, ethics, philosophy, and theology — at some 21 Canadian universities and 13 hospitals, clinics, and other institutions were involved in the research program.

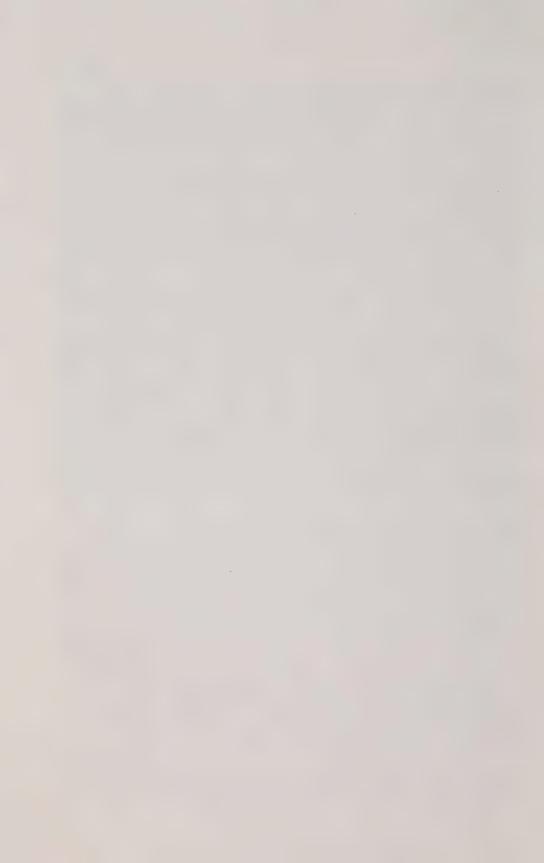
The Commission was committed to a research process with high standards and a protocol that included internal and external peer review for content and methodology, first at the design stage and later at the report stage. Authors were asked to respond to these reviews, and the process resulted in the achievement of a high standard of work. The protocol was completed before the publication of the studies in this series of research volumes. Researchers using human subjects were required to comply with appropriate ethical review standards.

These volumes of research studies reflect the Commission's wide mandate. We believe the findings and analysis contained in these volumes will be useful for many people, both in this country and elsewhere.

Along with the other Commissioners, I would like to take this opportunity to extend my appreciation and thanks to the researchers and external reviewers who have given tremendous amounts of time and thought to the Commission. I would also like to acknowledge the entire Commission staff for their hard work, dedication, and commitment over the life of the Commission. Finally, I would like to thank the more than 40 000 Canadians who were involved in the many facets of the Commission's work. Their contribution has been invaluable.

Patricia a. Baird

Patricia Baird, M.D., C.M., FRCPC, F.C.C.M.G.



Introduction



We are in the midst of a worldwide knowledge revolution with regard to reproduction and to genetics. The issues that are posed by the application of this knowledge revolution to the human situation are much more than health issues; they are societal, ethical, legal, and economic issues. How this knowledge is applied has the potential to change the nature of our society and how it views women, children, and the family, and it will have consequences in many sectors of our society.

The studies in this volume examine how some of these sectors — the science system, the industrial/commercial sector, the education system, and the social welfare system — relate to new reproductive technologies. Some, like the science and industry sectors, are involved primarily with the technologies' development and use. Others, such as the education system, are involved with the technologies' relation to individuals — individuals during their formative years, when there is the best chance to help young people assimilate knowledge and attitudes to help them protect their fertility and lessen their need for future use of new reproductive technologies. Still others, such as the social welfare system, have implications for and are affected by the existence and use of new reproductive technologies.

This volume complements Volume 2 of this series, which focusses on the social values and attitudes of Canadians concerning new reproductive technologies. Taken together, these two volumes provide an effective overview of the broad social context within which new reproductive technologies occur in Canada and make it clear that this context is not limited to medical or health care matters.

The Studies

Laurie Edwards characterizes the science and technology system in Canada today as an increasingly important social and economic force. He describes a three-way relationship between the research community, industry, and government, and he suggests that the public policy options open to government may be limited in terms of ensuring socially responsible management of the system. He states that part of the impetus must come from the scientific community itself, and that it is important to engage that community's sense of responsibility. Mr. Edwards present a paradox: as science and technology become more important and more central to the workings of modern Canadian society, less and less may be known or understood by the general public about how they work. This finding is especially significant in light of the concern and wariness Canadians display about the rapid pace of scientific and technological developments and the deficiences in public accountability and transparency to keep pace with these developments.

Canadians feel strongly that reproduction should not be commercialized, and they have a profound concern that commercial activities in the area of new reproductive technologies, particularly the activities of the pharmaceutical industry, should not be what determines policy and what is available in the field. Anne Rochon Ford, in her study of select forces in the development of *in vitro* fertilization, discusses the role that the pharmaceutical industry has played in the development and subsequent marketing of fertility drugs. As she demonstrates, the industry has its own goals; however, it does not act in a vacuum, but rather responds to social factors, primarily an increase in the call for infertility treatment. This increased demand is, in part, an outgrowth of the women's health movement and of a belief, arising from women's increased control over reproduction in terms of controlling contraception, that women who are unable to conceive have a right to seek help.

The influence that the pharmaceutical industry, with its development of hormones, has had on infertility treatments is not matched by the influence that infertility treatments have on the pharmaceutical industry in general. As Joyce Rowlands indicates, new reproductive technologies are but a tiny part of the broader pharmaceutical industry — of 3 000 medications listed in the *Compendium of Pharmaceuticals and Specialties*, only 8 are classified as fertility drugs. They also find that most research related to new reproductive technologies is conducted outside Canada, and that most firms do not find new reproductive technologies to be a large enough area to justify more attention in terms of investment and development.

This does not mean that the activities of pharmaceutical companies are irrelevant — indeed, one company, Serono, is responsible for 75 percent of the world's sales of fertility drugs, and the area of infertility treatment is extremely important to its market niche and profitability. However, the relatively limited extent of commercial involvement in new reproductive technologies compared to other areas of focus for the industry as a whole that Ms. Rowlands and her colleagues document means that it is unlikely that the concerns of those involved in infertility treatments — either

providing the treatments or using them — are going to have a great impact on the pharmaceutical industry as a whole. Therefore, the problems that Anne Rochon Ford documents — aggressive marketing of products, overutilization of drugs for more and more indications, the emphasis on developing new products with the goal of capturing market niches rather than conducting longitudinal studies of existing drugs — are relevant to the industry as a whole, but this market-driven approach will also apply to those few companies whose market niche is the treatment of infertility.

The next two studies in this volume focus on specific areas of commercial activity. Gillian Chaloner-Larsson and colleagues home in on a particular area of commercial involvement: the role of the biotechnology industry in developing products for prenatal diagnosis using DNA analysis. Their finding that the industry views Canada's universal health care and government policies as restrictive and a disincentive to expand their base of operations in Canada is interesting in light of the concern that Canadians have about commercial involvement in reproduction and their view that regulation is both necessary and desirable. The probes being used in Canada are produced in university research laboratories and have not yet been approved for marketing for diagnostic use. If, in future, diagnostic tests and kits are developed, introduced, and marketed successfully, a larger market potential and, therefore, changes in the role of the industry, could result.

SPR Associates surveyed 26 biotechnology companies in Canada, along with the 67 member companies of the Pharmaceutical Manufacturers Association of Canada, to discover to what extent and in what way reproductive tissues — eggs, sperm, embryos, ovarian tissue, abortuses/fetal tissues, and placentas — are used in research in Canada. Only one pharmaceutical company reported any research using a human reproductive tissue — in this case sperm — and the research was being conducted outside Canada. Fifteen percent of the biotechnology companies indicated that research was being undertaken using a human reproductive tissue; the research projects included the use of placentas and sperm, as well as the use of human cell lines originally derived from fetal lung fibroblast in the late 1950s and 1960s.

Throughout its public consultations, the Commission found that Canadians hold strong views about the role of the education system. The Commission heard repeatedly that the schools have an important role to play in preventing infertility and that not enough is being done in this area. The study of the education system by Shannon and McCall Consulting Ltd. confirms that there is a great deal that schools can do in terms of preventing sexually transmitted diseases among young women and men, so that they do not jeopardize their future fertility before they have even thought about having children. The study also makes clear how overburdened the existing school system is, and how difficult it will be to find the time, energy, and funding for programs that incorporate the content that is needed. The study also sensitizes us to the complex,

demanding, and often frustrating nature of health promotion initiatives aimed at changing the behaviour of adolescents. Most importantly, it points out that these initiatives are not usually successful unless located within the context of the broader community.

This broader community encompasses parents, peers, health services, and, importantly, the social welfare system. The programs that together make up this system have the ability both to affect and to be affected by the availability and use of new reproductive technologies. As Sherri Torjman reminds us, social welfare programs can work with schools and other bodies to help reduce the demand for new reproductive technologies by decreasing exposure to factors that cause infertility, particularly sexually transmitted diseases.

Importantly, Ms. Torjman reminds us that the effects of new reproductive technologies extend well beyond medical intervention and permeate everyday life. She notes that those directly involved in infertility treatment or prenatal diagnosis may be in need of significant amounts of counselling or other support services. Her discussion underscores that caring for people who are infertile or at risk of genetic disease is not the responsibility of the health care system alone, but is the broader responsibility of society as a whole.

Conclusion

It is clear from the studies in this volume that the task of fashioning a new and more socially responsible approach to new reproductive technologies will be impossible if it is perceived that the only necessary steps and the only needed reforms are concentrated in the health care system. The involvement of the various sectors profiled in this volume makes clear how inappropriate it is to try to categorize new reproductive technologies solely as a medical problem, or even as a medical problem with legal implications. Instead, new reproductive technologies are part and parcel of broader social issues concerning how we relate to one another, how we help each other through social services, how we educate our children to be responsible and healthy members of society, and how we create and maintain a balance between, on the one hand, scientific progress and commercial activity and, on the other, ethical use of scientific knowledge in a way that respects human dignity and is accountable.

The studies in this volume also show how the challenge of ensuring responsible development and use of new reproductive technologies requires a concerted approach that covers all of Canada and all the different sectors of society. To approach this challenge in a piecemeal, sector-by-sector manner will result only in a patchwork of measures that together do not provide the kind of national action and public accountability that Canadians are calling for.



Discovery, Community, and Profit: An Overview of the Science and Technology System

Laurie Edwards



Executive Summary

This document is an overview of the science and technology system from which the new reproductive technologies emerge. It describes the system as it relates to the new reproductive technologies, including the funding of science and the inter-relationships among the key players—the research community, industry, and government.

The paper delineates the ways in which science and technology are perceived by the various communities with an interest in them, including the people who use, consume, and criticize them. It discusses society's attitudes toward science in general and the reproductive sciences and technologies in particular.

Its conclusions encompass such areas as the interest of researchers and industry in reproduction, government's role in balancing public and private interests, and the social responsibility of the scientific community.

The document ends by suggesting issues for further consideration by the Commission as it deliberates on ways in which to influence the science and technology system.

This paper was completed for the Royal Commission on New Reproductive Technologies in April 1992, with contribution from Roger Voyer.

Introduction

The Royal Commission on New Reproductive Technologies, as part of its mandate, has to make recommendations on how Canada should deal with the social, moral, and legal implications of the new reproductive technologies. The recommendations undoubtedly will include suggestions for mechanisms to improve the accountability of science and scientists, health care professionals, and industry in the development and implementation of a broad range of the technologies. Indeed, the issue of accountability is the crux of this Commission's task.

The stakes are high and the timing precipitous, for advances in the life sciences are altering the very way we think about ourselves as a species in relation to the cosmos. Moreover, the technologies present unusual opportunities for abuse by individuals and groups. Still, while the dilemmas occasioned by the new technologies originate in the discoveries of science, the expertise, predictive capability, self-interest, and even the solidarity of researchers as a community are resources that can be turned to general benefit.

This is a field full of paradox and uncertainty. It is clear, for one thing, that while, as a culture, we are captivated by and materially dependent on science and technology, at the same time, as individuals, we are practically uninformed about them and what they do. This popular alienation puts everyone at risk, for it leaves us vulnerable on the one hand to simplistic solutions such as curtailing or shutting off certain technologies (strategies often tagged as neo-Luddite) and, on the other, to scientific and technological adventurism.

Of course, the perception that science is powerful, important, and dangerous is accurate. It has the potential for being all these things. In the past, a distinction was maintained between basic research and the application of scientific discovery (technology); it was not until the Second World War that the two activities were connected and equated in the mind of the state: governments had grasped the significance of technologies like broadcasting and nuclear power and had moved in to regulate them in the public interest. But in the 1940s and 1950s, the state also began to realize that investment in one (research) could actually produce results in the other (technology). Appreciation of the power of science led to the desire to control it.

The desire to control science can be viewed as an expression of the normal human fear of the unknown. It can also be understood as a reasonable response to the modern experience of technological development, which tends to trail human, environmental, and cultural damage in its wake. There has been an increasing public demand for the state to disallow certain avenues of research and investigation, accompanied by calls for the prohibition of already functioning technologies and scientific techniques.

Like the tendency to treat pornography through state censorship, the tendency to proscribe inquiry (as distinct from the application of technology) is dangerous — and for the same reasons. As scientist-philosopher Michael Polanyi warned in a Yale lecture entitled "The Tacit Dimensions of Understanding," "If you deny the power of thought, you deny the basis of freedom of thought."

In Western democracies, the state frequently sets out to broker vested interests within society on the theory, and with the expectation, that in the process the public interest can be represented. But as a regulator and legislator of intellectual endeavour, the state is a clumsy, blunt instrument at best: the regulator often becomes a captive of the industry or activity it is supervising, thus defeating its own purpose; the state often seems unable to prevent abuse in the application of its own laws. As writer Jane Rule (whose books have been routinely "censored" at the border by Canada Customs) puts it, "Parliament writes laws intending to get the Marquis de Sade and almost always gets Margaret Laurence instead."

Science, like art, flows from the imagination, and the essence of scientific investigation is curiosity. As soon as an external agenda is imposed, be it political, commercial, or moral, well-intentioned or no, the process is corrupted and the freedom of intellectual endeavour compromised. In Canada, we have traditionally sought to protect the integrity of scientists and their work by funding them at universities where their employment is protected by tenure. This, however, has not prevented the state from influencing the research agenda by channelling funds to areas in which it has an interest, and not to others.

Today the life sciences are generating extraordinary insights into the way living things work. The research universe has become large and complex and is evolving rapidly. While the amount of research on human reproduction is small, the field is integrally bound up with investigations that raise fundamental ethical questions about human interference in natural processes. Advances in a wide range of biological disciplines are forcing a reassessment of long-held assumptions about the sanctity of life, the meaning of human individuality, parenthood, the rights of people with disabilities, and the responsibility of the public to participate in decisions about the implementation of new technologies.

This reassessment comes after a period of substantial investment in the construction of science-based health care systems. Moreover, it is occurring against a backdrop of great change in the world economy. The globalization of trade and investment has intensified competition among corporations, nation states, and even small communities that try to attract wealth-generating industries to their regions. Evidently, any constraint on scientific advance and/or technological development will conflict with the imperative to create new knowledge and use it to make enterprises more innovative, productive, and competitive.

This means that if a country or a province or state decides to go it alone in introducing constraints on research and development, the cost will

be high. Restrictions will be interpreted by industry as an obstacle to growth, scientists and research funds will go elsewhere, and new products and processes based on research in the field will be developed elsewhere and perhaps be in sufficient demand that they find their way back into the domestic market anyway. This is not to dismiss or diminish the significance of the ethical issues and social critiques raised by the new reproductive technologies. However, it does mean there is a need to base regulatory and other means of controlling the development of the field on genuine sensitivity to the way science and the scientific culture work and to public attitudes toward science. In other words, there is a need to work with rather than against the scientific community in designing and implementing options for the control of the new reproductive technologies.

Science, Technology, and Society

Science is a way of knowing. It produces knowledge that has the capacity to change our understanding of the world and, therefore, our experience of life. Ever since God expelled Eve and Adam from the Garden, moreover, we have understood the connection between knowledge and power. For this reason, science, or more precisely scientific investigation, is and always will be a profoundly disturbing undertaking; it threatens to change the way we see things, to unleash unforeseen effects and energies into the universe, to disrupt the balance of power between people and nature.

Technology can be thought of as ways of doing things,¹ including science itself. As metallurgist Ursula Franklin argued in her Massey Lectures, "technology has built the house in which we all live ... All are affected by the design of the house, by the division of its space, by the location of its doors and walls ... And the house is still changing; it is still being built as well as being demolished."

Attitudes toward science range from the view that it is an instrument of human despair to the conviction that it is the midwife of the new millennium. Cultural history tells us that science has regularly and dramatically altered the way people viewed themselves and the cosmos. Scientific discovery, when assimilated, has brought revolutionary change: Copernicus, Kepler, and Galileo removed us from the centre of the universe; Newton turned God into a rationalist; Descartes trumped him by turning man into God; Darwin used the Frenchman's methods to demonstrate that human beings were more closely related to hairy apes than to any deity; Nietzsche announced the death of God, and then Einstein proved that nothing is absolute, not even time; Watson and Crick informed us that the building blocks of life are contained in a double-stranded helix of base chemical pairs; and nowadays we can hear the distant squabbling of Hawking and his colleagues debating the big bang theory of the universe's creation. Apparently, when Eve and Adam left the Garden, they took the apple with them.

Of course, scientific discovery has not always been received with equanimity. Church, state, and the Establishment have not always been pleased, and their resistance has sometimes been extreme. The Catholic Church imprisoned Galileo for his views, which it thought could bring down Christendom itself. Three centuries later, Darwin's ideas so enraged the Church of England that Bishop Wilberforce was dispatched to debate T.H. Huxley in a public meeting of the British Association for the Advancement of Science. (The bishop was odds-on favourite to win, but Darwin's ideas carried the day, the century, and the *zeitgeist*.)

Advances in reproductive science and technology can be expected to fuel our worst apprehensions. For example, an important ramification of advances in the field is the way they encourage physicians to conceptualize the fetus as a patient and thus a distinct entity from the mother. Prenatal surgery can now be used, for instance, to treat fluid build-up in the brain, blocked bladders, hernias, and other problems. This means that an adversarial relationship can be set up between the mother and her fetus.³

Reproduction is not, and has never been, a neutral subject; it is the point at which science and the church have repeatedly clashed, where feminist thought and religion have collided, and it should be no surprise that a royal commission on new reproductive technologies has become a lightning rod for all the preconceptions, misconceptions, and apprehensions about science and the scientific process. Everyone understands reproduction, most people experience it, and everyone assumes it is an integral part of ordinary human life. You do not need a science degree to reproduce, and having children is no guarantee of expertise in, much less wisdom about, the moral, social, and political issues reproduction entails.

There is therefore a tradition of political opposition to science, which has focussed on reproductive technologies encompassing, more or less frankly, an analysis of power. Theologians and feminist scholars and others have developed critiques of science, viewing it variously as the servant of the patriarchy, of commercialism, and of secularism. In part these critiques can be viewed as normal expressions of human caution. In part they must also be understood as expressions of the human desire to take responsibility — for the environment, culture, and the nurturing of the next generation.⁴

Science and the New Reproductive Technologies

The new reproductive technologies include those dealing with human conception such as *in vitro* fertilization (IVF), artificial insemination, and surrogacy (preconception arrangements), as well as embryo and fetal tissue research, prenatal diagnosis and genetics, and the causes and preventions of infertility. Underlying the technologies are advances in the basic life sciences of physiology, morphology, endocrinology, developmental biology, biochemistry, and molecular biology. ⁵ Increasingly sophisticated electronic and computer technology, together with progress in molecular biology, is

constantly increasing the rate of discovery and development in these and related fields.

According to the Office of Technology Assessment (OTA) in the United States, the foundations of modern human reproductive biology were laid in the 1930s when the field of endocrinology experienced important breakthroughs in the understanding of the reciprocal relationship between the pituitary gland and hormonal control of the ovaries and testes. The OTA points out that in the 1960s radioimmunoassay techniques enabled scientists to measure minute amounts of reproductive hormones, permitting the characterization of both normal reproductive health and pathology. By the late 1970s, research on contraception and fertility had led to the identification and purification of numerous natural and synthetic reproductive hormones. Research on mammalian eggs and early embryos intensified, aided by advances in non-human IVF and the preimplantation development of fertilized eggs.

By 1988, when the National Academy of Sciences (NAS) in the United States set out to create an agenda for research in assisted conception, animals were being used to test a wide range of related technologies. Besides IVF (already being used for people), they included superovulation, embryo transfer, freezing, sexing, multiplication (by bisection and cloning), and modification (by gene transfer). Meanwhile, novel reproductive procedures, based on inventions in microsurgery, optical fibres, and ultrasound technologies that permit routine visualization and retrieval of

human eggs, have quickly moved into clinical application.8

Fetal research has also proceeded apace and has produced improvements in the invasive and non-invasive diagnosis of fetal disorders (metabolic and congenital) and the treatment (including surgical intervention) of disorders. And fetal *tissue* research is used for testing the efficacy of vaccines and the titration of drugs and has benefited a number of biomedical areas by providing cell lines to study gene regulation, pattern formation during embryogenesis, and model systems for cell interaction and function. The drug companies that use fetal cells for screening new pharmaceutical agents to determine their risk as teratogens or carcinogens report that "these experiments are essential before clinical trials may be undertaken." Transplanted fetal tissue has also shown great promise in the treatment of diseases involving the destruction of tissue, such as nerve tissue, that regenerates with great difficulty, if at all. This treatment has already been used for Parkinson's and Alzheimer's disease, for example.

Notwithstanding these advances, some scientists are concerned about a number of impediments to research. A 1989 report of the Institute of Medicine in Washington, D.C., identified deficiencies in the scientific base of assisted conception, inadequate resources for research and materials for experimentation, and a lack of communication among basic researchers, clinicians, and animal husbandry scientists. Public suspicion of reproductive technologies and fear of their abuse, a lack of public sympathy for couples experiencing infertility, and the absence of organized public

support favouring the research, as compared to the well-organized opposition to it, are also cited as factors that inhibit research on human reproduction in the United States. These factors also apply in Canada.¹²

Of course the response of the scientific community to the social and political impediments to research can make them into self-fulfilling prophecies. Once an area is known to be problematic, the best researchers are likely to avoid it, and those left in the field are unable to compete successfully for research grants. In science, as in medicine, there are vogues in research, and some fields have greater prestige than others.

As things stand, reproductive science has little cachet within the basic research community, in Canada or the United States, and the statistics on research spending and personnel reflect the situation. In 1990, the Medical Research Council of Canada's contribution to research in the field was \$7.1 million, 4.5 percent of its research budget. By way of comparison, in 1986, in the United States, approximately \$155 million was spent on research into human reproduction, of which \$109 million came from the \$5 billion budget of the National Institutes of Health (NIH). 14

There appears to be a decline in the number of scientists moving into the already small field of new reproductive technologies in the United States. ¹⁵ In Canada, 61 principal researchers at Canadian universities and hospitals received Medical Research Council grants for research related to the new reproductive technologies in 1990-91 (see Figure 1 for a list of grantees). ¹⁶ The Medical Research Council awards some 2 900 grants to principal investigators each year for all fields of research.

Molecular Biology — A Special Case

These numbers do not include genetics, which is the field where research advances are being applied in ways that raise the most profound social and moral questions. With extraordinary rapidity this science is finding new avenues for human interference in the natural reproductive and biological processes at the cellular level. Such interference can take the form of predictive technologies (screening for carriers of a genetic disease), diagnostic technologies (analysis of fetal cells for genetic abnormality and other characteristics such as sex and predisposition to disease), or therapeutic technologies (possible modification of the genetic make-up of somatic or germ cells to correct for deficiencies in the developing fetus).

Advances in human genetics and in many of the once-basic sciences such as biochemistry and physiology, which are actually concerned with translation of genetic information into the diverse functions of the living cell, are rooted in molecular biology. Biology went molecular, as it were, in 1953, with the discovery of the structure of deoxyribonucleic acid (DNA). After James Watson and Francis Crick's description of the double-stranded, helically shaped master molecule, physicists and statisticians as well as biologists and chemists concentrated in growing numbers on unravelling

the secrets of sequentially stored genetic information. The discoveries made since the Watson-Crick breakthrough have transformed the life sciences and blurred the distinctions once made among scientific

disciplines.17

What makes molecular biology so transformative is the way it allows science to understand living organisms from the inside out. According to one group of senior molecular biologists, research in the field has two principal thrusts. "First and oldest, beginning in the 1950s, is the study of the structure of molecules and the relationship of structure to function ... Second, beginning in the 1970s with studies of bacteria and their viruses, thence spreading throughout the biological kingdoms, is the manipulation and purification of genetic material and through this the understanding of gene structure, expression and function ... as a way of thinking about life processes it [molecular biology] is the leading paradigm of the decade." 18

Not only has doing biology at the molecular level expanded the horizons of the life sciences, it has accelerated the process of discovery. This is so because recognition of its potential has led to proportionately more energy and resources going to the life sciences, the application of other technologies (particularly computers) to biological problems, and the automation of time-consuming bench tasks. To take one illustration of this acceleration, since 1975 the number of sequences of base pairs on the human genome that have been published (entered into GenBank, EMBL, or other bases for data on human genetics) has been increasing at the rate of 60 percent a year.¹⁹

Because of the molecularization of biomedical science and the speed-up of scientific advance, industry has changed its habits; to be competitive these days, it must primarily develop products and only secondarily worry about markets. Gordon Postlewaite, Executive Director of the Pharmaceutical Manufacturers Association of Canada (PMAC), says that "unlike traditional forms of drug research which are disease driven ... biotechnology is technique driven, meaning it tends to be more R&D intensive."²⁰

The possibility of genetically predicting and explaining human characteristics is perhaps the most worrying social implication of advances in the biological sciences. Despite the inaccuracy of overly simplistic "body as machine" models, their perceived potential for explaining learning disabilities and behavioural problems in simple biological terms speaks to society's ever-present interest in predictive information. Such models, which tend to ignore the complex interactive web of causation that obtains among genetic, social, emotional, and biochemical background phenomena, "are particularly appealing in school systems pressed by demands for efficiency and accountability." The models are based on advances in molecular and behavioural genetics and may sometimes assist in the early identification of problems such as dyslexia and perhaps in the development of remedial programs. ²²

The molecularization of medical science illustrates the tendency of scientific events to overtake and in some instances to be used in redefining social and ethical issues.²³ Jay Moscowitz, Associate Director for Science Policy and Legislation at the NIH in Washington, noted recently that work on "designer cells" was proceeding so rapidly that the controversial use of fetal tissue for research²⁴ may soon become irrelevant because there would be little need for the "real thing."²⁵ However, while this may be good news to critics who worry about the possibility of science coercing women to abort fetuses for research, an underlying but different issue of engineering human material still remains. 26

Part 1. The Science and Technology System

The new reproductive technologies are being developed within the context of a complex science and technology system. This system manifests society's commitment to science in general. Broadly speaking, the social commitment to science includes the assumptions that prowess in research is a social good and that science and technology can be relied on to achieve social objectives. These assumptions are given new force by the growing realization that scientific and technological capability is a key factor in economic development, especially in the context of the rapidly emerging global economy.

In this section we examine these assumptions and the role of science in the economy, describe the culture of the research community, and explore the roles of government and industry in the science and technology system. The section concludes with a description of Canadian research expenditures and the roles of government and industry in the promotion and regulation of the life sciences and the technologies that are based on them.

Science as Social Good

The prestige accorded Nobel prize winners John Polanyi and Gerhard Herzberg is indicative of the admiration inspired by scientific achievement. Universities rate each other, for the most part, by reference to the quality of their researchers, not the quality of the teaching their institutions provide. It is known that some universities in the United States use the number of Nobel laureates on their science faculties as a benchmark in strategic planning. Governments have also begun to rely on quantitative criteria, such as the number of scientific publications and citations, for the measurement of research performance as a way to differentiate postsecondary institutions; the United Kingdom recently undertook a wholesale restructuring of its support for universities using such an analysis, and here in Canada, the Royal Society has been given funds by the federal government to evaluate research output. Public laments about scientific illiteracy and the poor quality of scientific education in Canada compared with Japan, Germany, and other OECD (Organisation for Economic Cooperation and Development) nations manifest the belief that scientific competence is the hallmark of an advanced society.

We are used to depending on science and technology. Not only do high-technology products and services permeate everyday life, we put our faith in the ability of new technologies to cope with the future. We believe scientists when they say there is a hole in the ozone shield, when they explain the existence of a worldwide warming trend as being due to the buildup of carbon dioxide in the atmosphere and the dangerous depletion of the planet's oxygen because of the disappearance of forests. We sigh with relief when we hear that genetically engineered bacteria can absorb excess carbon dioxide and may be able to consume the pools of industrial waste in polluted water supplies. We grow impatient when scientists explain that the war on cancer will take more than a single campaign, while government lectures the business community about the need for it to put more money into research, and everyone lectures government about the need to spend more. There is a widespread feeling that as a society we need to know more — about our environment, our markets, our resources, our bodies, our diseases. You could say that Western culture is scientifically anxious.²⁷ Over the years in the so-called developed world, this anxiety has translated into a significant financial investment in research and development.

Over the last 30 years there has been a remarkable worldwide growth in the financial commitment to the life sciences in particular, a trend driven primarily by the desire to improve medicine. Health care in several countries has long been considered the government's duty to provide and the citizens' right to receive, so biomedical research has generated significant public expenditures in Canada and elsewhere and is widely considered as not only a budgetary but a political fixture of modern advanced societies. Figure 2 compares government expenditure on health care research and development in Canada and selected other countries. The figures for Canada include provincial governments.

The main factors that motivate nations to invest in research are usually the following: the desire to reduce expenditures on health care and their perception of medical advance as the route (think, for example, of the savings generated by one vaccine, the Salk vaccine for poliomyelitis); the need to be technically competent to effectively manage and regulate innovations originating in other countries; and the belief that research in this field will lead to industrial competitiveness. It is noteworthy that agencies that fund medical research on society's behalf are increasingly being asked to demonstrate and produce economic benefits. The NIH in the United States is the largest single funder of medical research in the world²⁸ and has recently drafted a mission statement that includes as one of four overarching goals the provision of "the scientific base that will strengthen

the Nation's economic competitiveness and ensure a continued high return on the public's investment."²⁹

It should be noted, however, that dedicated funding of reproductive science and technology in the United States³⁰ has not been significant, and the field could hardly be construed as being an important factor in the global competitiveness sweepstakes. In 1988, approximately \$115 million was spent on research into human reproductive processes in the United States. Private foundations contributed slightly more than \$2.8 million. One of the national institutes, the National Institute of Child Health and Human Development, typically spends about one-third of its budget on reproductive science.³¹

Globalization of the Economy

Escalating development costs coupled with the lowering of trade barriers protecting domestic markets from unrestrained foreign competition in more and more sectors of the economy have been forcing firms in Canada and elsewhere to rely increasingly on sales in international markets. Domestic markets in most countries are no longer large enough to support product development in many science-based, high-technology areas such as medical devices, biotechnology, and pharmaceuticals. These areas are the growth sectors of the future, and a country's performance in them is becoming an important determinant of its economic health.

On a worldwide basis, technology-intensive trade is expected to top \$1 trillion by 1995, representing about 28 percent of world trade (up from \$320 billion in 1980, when it was about 10 percent of world trade). This growth is fuelled not only by greater emphasis on the export of goods and services but also by the increasing mobility of the capitalization, research, design, development, production, and marketing functions of the modern corporation. Firms that want to sell products internationally now tend to establish a significant presence in their target markets. Since 1985, at least, this trend has been developing and has resulted in worldwide (foreign) investment growing faster than trade itself (Figure 3).

Investment can take many forms. It can be a manufacturing plant, a strategic alliance with local firms, or a commitment to research and development. In the 1980s, business financing of research and development in OECD countries grew at a rate 50 percent faster than that of government financing. Some of the money was invested in research programs or projects at local universities. In 1980, for example, Harvard University accepted a "donation" of \$50 million over 10 years, through Massachusetts General Hospital, from the German pharmaceutical firm Hoechst to establish a research department in genetic engineering. Hoechst retains exclusive world rights to license any new developments. Not to be outdone, Stanford and the University of California at Berkeley have formed a Center for Biotechnology Research with funds from six chemical, engineering, and biotechnology companies.

The strategy of scanning the world for scientific and technological capabilities and investing in them wherever they are located is being implemented by large companies everywhere and has even been given a name by the consultants, bureaucrats, and managers who specialize in planning, facilitating, and designing strategic alliances. It is called "search and develop" (as distinct from research and development) and is an important influence on the science and technology system, since it sets off a fierce competition among political jurisdictions and between academic researchers to attract investment into their communities and projects.

The Research Community

Research can take many forms and be undertaken in many circumstances. In the life sciences there is room for statistical experts, clinicians, experimentalists, and many others. By 1990-91, there were 8 000 scientists doing health research in Canada, of which 2 900 obtained peer-reviewed grants from the Medical Research Council.³³ The research community also includes a great many people who participate in a supporting or ancillary role, including technicians, graduate students, information specialists, industrial designers, and others. These people are employed by universities, hospitals, industry, or government.

What scientists do is research. Research is "the continuous, disciplined advance from the known into the unknown."³⁴ The object of research is usually technical and "dependent for its meaning and significance on the context of the existing information in the special field."³⁵

Good science must be significant as well as competent in experimentation and observation. Above all, it must be original. This means completing the research, writing up the results so they can be verified and replicated, and getting them published or presented in a credible forum before anyone else does. Excellence is not just a slogan in science, it is the prerequisite for survival.

Modern science is one of the most competitive activities ever invented. To begin with, predictably, the number of scientists competing for research grants has increased faster than the grant monies and facilities available. In the United States, which drives the research system globally because of the sheer size of its investment in science, between 1980 and 1988, "scientists and engineers in the work force grew by an average of 7.8 percent per year, four times the annual rate for total employment." At the same time, the outlets for publishing descriptions and findings, the scientific journals that subject new work to the scrutiny of peer review, have not kept pace with the quantity of research being done. These days, moreover, research techniques depend on increasingly elaborate and expensive technologies for the measurement, manipulation, and recording of data, access to which is itself highly competitive. The attrition rate of qualified people able to undertake and sustain significant research projects is exceedingly high.

It is debatable whether the extraordinary advances of modern science are due more to the power of the scientific method or to the fierce competition governing the everyday lives of its practitioners.³⁸ Of course, this does not mean that scientists are not also idealistic and deeply committed to the scientific process and its benefits.³⁹ Whatever the case. one would not expect to find the virtues of cooperation and sharing in such a community; on the contrary, it has been argued that science as an activity emphasizes hierarchy and authoritarian rule. Nonetheless, scientists do belong to a functioning community and do share certain values over which they can be expected to collaborate and cooperate.

Most scientists are conservative: good followers. philosopher Thomas Kuhn has noted, is to flesh out the ideas and articulate the paradigms that have already been accepted. If experimentation does not demonstrate the applicability of a paradigm, the likelihood is that the experiment has been wrongly conceived, for at that level it is unprofessional for carpenters to blame their tools. For the ordinary and applied scientists, the challenge is to work within the most thoroughly conforming part of the paradigm, but quickly, efficiently, and toward a highly focussed goal. Paradigms are questioned only when the complexity of making experimental evidence fit the paradigm demands such virtuosity and encyclopaedic knowledge that the pressure for a new perspective becomes irresistible, or because maverick thinkers who teeter on the edge of credibility decide to blame the tools and find something completely different to work with to survive the inevitable accusations of heresy.

The progress of modern science owes a great deal to those journeymen researchers, the practitioners of Kuhn's "normal" science. Paradigms can be articulated quickly because of the rigours of competition, which demand strict discipline and concentrated work. How else in a single year could the identification of the gene responsible for cystic fibrosis be followed by the discovery of how that gene expresses itself? Such is the power of normal science.

As science becomes increasingly high tech and equipment costs for research escalate, the dependence of researchers on special funding programs grows accordingly. One consequence is the growing reliance of university-based scientists on private sector sponsors. Many people worry that the academic requirement for openness and the sponsor's interest in proprietary rights conflict, and that the traditional independence of university science is threatened by the trend. The concern is widespread; a survey of American universities (Figure 4) demonstrates the wide range of policies that this conflict has generated in the research community south of the border where most research into human reproduction takes place.

Technology typically emerges from the creative meeting of scientific discoveries and ongoing industrial activity. The drive to develop technology can originate in the pressure to solve a problem, the entrepreneurial recognition of an opportunity to make money from research results, or the desire of investigators to be sponsored by large firms possessing an interest

in commercial applications and the research infrastructure needed to support competitive science. As basic research and technology development merge in transformative fields such as molecular biology, skilled academic scientists can be expected to move more frequently into the private sector.

Recent advances in molecular biology have triggered the formation of new biotechnology firms, many of them dependent on links to university researchers. The field of biotechnology has been responsible for the creation of quite new research structures. This is partly because the potential rewards are so great and partly because the industry is so dependent on fundamental and therefore speculative research. Venture capitalists join forces with basic researchers in the new companies and in so doing provide the scientists with resources that may not be available within academic institutions. This is more than sponsorship, of course; it is partnership in proprietary ventures.⁴⁰

In sum, scientists are driven by the need for recognition and scientific curiosity. As the globalization of economic activity continues, scientists who work at the frontiers of strategic areas of research, like molecular biology, are able to earn large fees from private sector clients. By going private and setting up their own companies or participating in joint ventures with others, they are also able to attract more support for their research programs from outside investors than would be available through traditional institutional channels. More scientific information is becoming proprietary.

Government

The role of governments is to work for the welfare of the people in their jurisdictions. On the one hand, this means promoting economic and industrial development to create wealth and employment. On the other, it means providing the regulatory framework within which industrial activities can take place in ways that enhance and maintain the welfare of their people. These responsibilities often conflict.

In most countries, governments have been the principal funders of basic research. For its part, industry has concentrated attention and resources on the development of new products and services or on improving the processes of manufacturing and resource extraction. Today, however, everyone is preoccupied with the link between research and innovation, and governments are responding with diverse development programs. Nor has it gone unnoticed by governments at all levels that some jurisdictions are profiting disproportionately from the "search and develop" strategies of transnational corporations. These are the jurisdictions where there are local clusters of science and technology capabilities. There are many such environments in the United States (see Figure 5). The most active nations are those that spend the most on research and development and have high concentrations of researchers. Canada, by contrast, traditionally reliant on trade in commodities, is a relative newcomer to high-technology develop-

ment and has few technology-intensive centres (see Figure 6 for a compar-

ison of the technology-intensiveness of Canadian cities).

There is intense competition among governments at the subnational level to build on existing technology strengths. The competition takes many forms, including tax incentives, relative freedom from regulatory constraints on research and the commercialization of technology, development grants, and boasting about the natural advantages of this or that region. An example in Europe is the Rhône-Alpes in France; the region has an especially aggressive strategy (including an office in Montreal) to attract international investment. 42

Technology-intensive "clusters" can also be *created*. Newly industrializing countries such as Korea, Taiwan, and Singapore have begun using this strategy. Concentrating on repatriating highly skilled nationals who have been trained and/or are working in the United States and Europe, they offer high salaries, large research budgets, and state-of-the-art facilities.

The controls exercised by society over research and the introduction of new products and services vary considerably from country to country. Indeed, these controls can be used as non-tariff trade barriers to protect domestic enterprises from foreign competition. As they do with labour costs and environmental standards, transnational companies can be expected to concentrate their investment in research and development in jurisdictions where the obstacles — in this instance, to innovation and commercialization — are least onerous (assuming other investment criteria are satisfied).

Of course, companies with their eyes on the global market tend to develop the actual products and services in such a way that they meet the regulatory criteria that obtain in the largest and most lucrative markets. This imperative, together with the need to satisfy first the requirements of the jurisdiction in which the product or service is developed, means that the research and development phase can be time-consuming and expensive. It can take more than a decade for a drug to get through the research, development, testing, and approval phases in Canada, for example, with costs in excess of \$200 million (see Figures 7 and 8). Most other industrialized countries have similar procedures.

As with the other areas of the life sciences, the control of research into reproductive biology varies widely from country to country. Mechanisms include the recommendations advanced by various studies and commissions, voluntary guidelines, and specific legislation. In the West, Germany and Sweden appear to be at the study and recommendation stage, while Australia (federal), France, and the United Kingdom have opted for voluntary guidelines. The United Kingdom has also established a Voluntary Licensing Authority. In the United States, there is an unofficial but effective moratorium on federal funding of research on IVF; the moratorium has been in place since 1980. Several American states have statutes regulating fetal research. These laws have broad application, but

the language is vague, and there is debate about their validity. In Australia, the states of Victoria and South Australia have passed legislation to regulate research.

Industry

The job of business is to stay in business and make the best possible return on investment for shareholders. Two business sectors have an interest in research that can relate to the "birth industry" — the medical devices sector and companies like the established pharmaceutical companies and the emerging biotechnology firms.⁴³

The devices sector is driven by the need of medical professionals for customized solutions to specific problems.⁴⁴ Typically, a biomedical engineer is consulted by the health care provider, a solution is found, and a prototype device is made. Usually, there is little interest in

commercializing these innovations.

The story for the emerging biotechnology industry is different. The 1970s and 1980s were an era of start-up companies based on partnerships between scientists and venture capitalists. Many of the survivors of this highly speculative era are now listed on the stock market, which is showing signs of a significant renewal and broadening of investor interest in the industry. Since January 1991, biotechnology firms have raised more than \$2 billion on Wall Street, double the amount for all of 1990. Share prices have soared (see Figure 9), expanding the capital resources of the 23 publicly traded firms in the widely used Oppenheimer biotech index by 64 percent to \$18.9 billion.

One of the reasons for this surge in investor enthusiasm is the interest that the transnational pharmaceutical companies are showing in the sector. Strategic alliances between long-established pharmaceutical companies and the newer biotechnology firms spread the risk of speculative, research-based product development⁴⁷ and help ensure that the mature companies remain at the leading edge of new, potentially competitive technologies. Some 55 percent of the 304 strategic alliances formed by transnational drug manufacturers in 1990 were with biotechnology firms, compared to 30 percent of the 124 agreements made in 1986. The alliances often involve large amounts of money: the biggest deal was Hoffmann-La Roche's \$2.1 billion purchase of a 60 percent stake in Genentech.⁴⁸

This kind of investment reflects the industry's conviction that the market for products based on advances in molecular biology will be enormous. However, except for genetic diagnostic kits and other products and services that have to do with screening for disease and predisposition to disease, it should be noted that the market for new reproductive technologies, most of them related to fertility, is in this context likely to be limited. There is unquestionably an opportunity to develop niche products, such as male and female contraception products for the 15 to 44 age group, or infertility treatments for the less than 10 percent of couples of child-

bearing age who are unable to have children. And there are several services associated with the new reproductive technologies (for example, infertility clinics and banks for the preservation of sperm), but the market

for such services is small. 49

Both the established pharmaceutical industry and the emerging biotechnology sector are leery of areas rife with contentious moral and social issues — such as human reproduction. The limited market potential and the sensitivity of this area, then, mean that it is not likely to be a major factor in the research strategies of the industry.

Research in Canada

Total expenditures on research and development of all kinds by *all* public and private sponsors in Canada have grown from a total of \$458 million [1990 dollars] in 1963 to more than \$9 billion in 1990. Government's share of gross expenditures on research and development in Canada is 45.8 percent, somewhat less than in the United States (50.8 percent) and France (52.9 percent). The Science Council of Canada has estimated a total expenditure by Canadians on health research of more than \$400 million in 1988-89.

The proportion of health care research and development compared to the total research and development financed by governments in Canada is 7.9 percent. In the United States it is 11.9 percent, two to three times more than in other countries, such as the United Kingdom (4.3 percent), France (3.6 percent), and Japan (2.4 percent). Expressed as a percentage of gross domestic product, funding for health care research and development by Canadian governments is greater than that in other major industrialized countries except the United States, which invests three times as much in the field (see Figure 2). In dollars, government support for health care research and development in Canada, at \$224 million (U.S.), is almost 10 percent less than in Germany (\$246 million) and Japan (\$240 million).

Government funding of the health sciences includes the expenditures of the Medical Research Council, the federal Department of National Health and Welfare, and provincial agencies such as the Alberta Heritage Fund. The Medical Research Council is Canada's most important sponsor of research in the health sciences. Its contribution to research into human reproduction in 1990 was \$7.1 million, about 4.5 percent of its research budget for that year.⁵² This compares with such leading fields as neuroscience (16.2 percent), biochemistry and molecular biology (11.5 percent), and cardiovascular sciences (7.4 percent). In 1990-91, 61 principal investigators (about 2 percent of investigators awarded grants by the Council in that year) at Canadian universities and hospitals received grants for research into topics identified by the Medical Research Council as pertinent to reproduction.

The federal government also has a \$240 million program of university-based Networks of Centres of Excellence to strengthen the research base

in selected areas. Two of the networks bear at least peripherally on the new reproductive technologies: the Genetic Basis of Human Disease and the Neural Regeneration and Functional Recovery networks.

Universities are responsible for much of the research done in Canada. Much of it, about \$1 billion, is externally sponsored, with a growing proportion of the funding coming from non-federal sources. "Non-governmental organizations have been a particularly significant source of funds for medical research ... By 1989, in fact, those [federal] granting councils provided only slightly more than half of the total university research sponsorship," according to the Royal Society of Canada in a recent report on university research. Done example of this trend is the fact that sponsorship of research by provincial and national not-for-profit foundations at faculties of medicine rose from around \$20 million to just under \$100 million annually between 1981-82 and 1989-90. In the same period, the private sector increased its share of biomedical research funding from 2.2 percent to 8.3 percent.

By the end of the 1980s, not only had the funding base of Canadian university research expanded greatly, it had changed in nature. In the last decade, more and more of the government funds for research have been earmarked for programs designed to stimulate industrial development. Emphasis on linkages between university research and industrial development has become pronounced in the policies of the federal granting councils. In 1983, the Natural Sciences and Engineering Research Council (NSERC) began to match grants made to universities by industrial donors: by 1989, the program had grown from \$2.5 million to \$25 million. In 1985-86, the federal government started tying increases in the budgets of the granting councils to matching funds from the private sector. The Medical Research Council subsequently introduced a program similar to that of NSERC. Moreover, since Parliament passed amendments to the Canada Patent Act (Bill C-22) in 1986, the pharmaceutical industry is obliged to invest large sums in research at Canadian universities, and the Medical Research Council has worked increasingly closely with this sector in the funding of biomedical science.⁵⁵

Many policy makers believe that stimulation of research in the pharmaceutical industry has been a signal success story. The reasons are not hard to find. The new research projects have put a lot of scientists to work in Canada, including a number of talented ex-patriots. Total annual research and development expenditures by the pharmaceutical industry, which consists of about 150 firms with shipments of some \$3.5 billion (1990), jumped from about \$70 million in 1986 to \$266 million by 1990, mostly in Ontario (43.3 percent) and Quebec (47.3 percent). While applied research dominated, most of it devoted to pre-clinical and clinical trials, basic research accounted for 26 percent of these companies' research expenditures. The total expenditure figure constitutes a research-and-development-to-sales ratio of 8.8, a little more than half the ratio in the

United States, where the industry estimates expenditures of \$9.2 billion for research and development, or 17 percent of sales in 1991. 57

The other big spender on research and development in the health care sector is the biotechnology industry. In 1988, the 218 Canadian-owned firms — most of them small and 120 of them in the health care sector — reported expenditures of about \$360 million, \$124 million (34 percent) of which related to health care. ⁵⁹ It should be noted, however, that there is some overlap with the expenditures of the pharmaceutical industry, and that only a few of the biotechnology firms that are active in the health care sector (for example, Allelix Diagnostics and Quadra Logic Technologies Inc., which make pregnancy and ovulation kits) have as yet developed new reproductive technologies or related products. For its part, the medical device industry expended an estimated \$45 million on research and development in Canada. ⁶⁰ This represented about 7 percent of sales for the sector's 650 firms.

Governments at all levels in Canada have aggressively supported science-based industry. Privately owned companies can take advantage of most government research programs either directly or indirectly through the provision of matching funds to universities or other research institutions. They enjoy a wide range of federal support programs such as the National Research Council's Industry Research Assistance Program, which provides direct assistance to small firms. As well, there are tax incentives for research and development.

Provincially, there are several striking examples of public investment in the development of a competitive science base in the medical area. Alberta has poured funds into programs to attract and support the work of outstanding biomedical scientists; the Alberta Heritage Foundation for Medical Research and the Alberta Cancer Board together provided \$23.5 million to faculties of medicine for research in 1989-90. Quebec has set up a provincial counterpart to the Medical Research Council and has worked hard to create conditions that would make the province an attractive place for the international pharmaceutical industry to locate research facilities and sponsor research. Fonds de la recherche en santé du Québec (FRSQ) provided \$32.9 million to Canadian faculties of medicine in 1989-90, second only to the Medical Research Council itself, which provided \$174 million to faculties across the whole country.

There are also provincial activities designed to develop links with foreign companies and attract investment to existing technology-intensive "clusters." Quebec has a Memorandum of Understanding (MOU) with France and Belgium (Flanders/Wallonia) on technological and industrial cooperation, for instance, while Ontario has signed similar MOUs with Rhône-Alpes in France, Baden-Wuerttemberg in Germany, Lombardy in Italy, and Catalonia in Spain; Alberta has an agreement with Flanders and Wallonia. The provincial research organizations, such as the Centre de Recherche Industrielle du Québec (CRIQ), ORTECH in Ontario, and the

Alberta Research Council (ARC) also have agreements with many of their

counterparts abroad.

Several of the larger Canadian municipalities with concentrations of scientific personnel (see Figure 5) are promoting this fact in their campaigns to attract industry and investment. Metropolitan Toronto, for one, has a professional development office dealing exclusively with the pharmaceutical and biotechnology industries; Ottawa has developed a "Biotechnology Business Development Initiative" to attract major international firms to the region. Also, there are more than 200 twinnings between Canadian cities and foreign counterparts. Increasingly, these agreements go beyond the usual political and cultural formalities to include technological and industrial cooperation. For example, the City of Windsor has an agreement with St. Étienne in France concerning the manufacture of plastic moulding, and there is an annual trade show that is held in alternate years in the two cities. Ottawa-Carleton has an agreement with the Hague, Netherlands, which has resulted in strategic alliances between firms in both places.

Regulation of Research and Health Care Products in Canada

Like several other countries, Canada has opted in the main for voluntary guidelines to regulate research (see Figure 10 for comparisons). The Medical Research Council advises prudence in the imposition of legislative controls on research "particularly in areas that are rapidly evolving. It is the view of the MRC that the interests of the Canadian people are best served when research is permitted to thrive in an atmosphere of freedom, tempered by the application of guidelines." ⁶³

Guidelines can lead to exacting review processes, as is evident in the history of a proposal for fetal tissue transplantation. The proposal in question was advanced by Dalhousie scientist Allan Fine. Dr. Fine moved to Halifax in 1987 with the intention of doing his research on a clinical basis and made his proposal for ethical approval in early 1988.

It went first to a University research committee, which granted approval early in '88. Then, later in '88, end of the summer, it went forward to the Victoria General Hospital's Institutional Review Board, the first stage in their review process, and there it was given what was the longest and most detailed assessment in their history. It took about a year and a half for a decision to be reached, at least to be communicated, and that decision was finally positive. I hope that we'll have more information available to you from the people who are on that review board. We who submitted the proposal kept fastidiously apart and so I can't give you details about the pressures brought to bear upon them.

I can give you information on the pressures brought to bear on me and other members of our team, during the period since the first news reports of this proposal were published. I and other people have received a steady stream of letters and telephone calls. A few of them have been supportive, the majority of them have been hostile, and they range from

courteous expressions of disagreement to outright hate-mail, including such things as pictures of decapitated fetuses, letters describing us as Nazis, and blots on the honour of the medical profession.

I'm happy to report that those negative pressures were successfully resisted, and approval was granted by the Institutional Review Board. There were several other steps in the review process before any actions could be taken of a clinical sort. These included review by a scientific and medical committee in the hospital, and then by executive boards in the hospital. We were not able to do anything clinically, not even to collect fetal tissue to get the actual practical aspects under way, until that approval had been granted.⁶⁴

The example illustrates how the guidelines of the Medical Research Council (see Appendix 1) are adhered to within both the university and the hospital research contexts.

The Health Protection Branch of the Department of National Health and Welfare is the focal point for the regulation of health care products in Canada (see Figure 11). The branch has an established network of outside experts to augment its own internal expertise. At times, it establishes expert advisory committees. It also has ongoing contacts with professional organizations, associations, and consumer groups, and through this web of consultations the branch establishes regulations and evaluates and monitors developments in the field. Because companies must submit their clinical trial data to the branch to get approval for new products, there is an opportunity for the government to scrutinize industry compliance with standards for research practice. These include the guidelines of the Medical Research Council. 65

It is the industry that puts pressure on the branch for "due diligence." This is because companies that have already gone through an expensive development phase when they apply for the branch's approval are anxious to get their products onto the market with as little delay as possible. The pressure is obviously intense with pharmaceuticals⁶⁶ because of the drawnout developmental stage that is involved in the creation of a new drug, a stage that effectively abbreviates the period when the company concerned is protected by patent law. ⁶⁷

Part 2. Perceptions of Science and Technology

The effectiveness of the polity in changing the way the development and use of new technologies are controlled depends on the attitudes of society toward science. Attitudes are especially critical if the science behind a technology has broad applications, is thought to be strategic in that its progress will drive advancement in other fields of research, or challenges fundamental assumptions and social values. These conditions

clearly apply to the science and technology of human reproduction,

especially those based on molecular biology.

Attitudes toward science and technology can be considered in terms of three broad perspectives: the managerial perspective, the perspective of the consumer of science and technology, and the critical perspective. These are discussed below. Because the most informed and articulate expressions of concern about the social and moral impacts of reproductive science and technology originate with the last of these, in this section of our overview of the science and technology system we concentrate on the critical perspective.

The Managerial Perspective

Managers, be they in government or industry, understand the world in terms of means and ends. In most Western countries, medicine is the prime example of how science can be turned to social objectives, and the share that health care research has of national budgets reflects this. Moreover, as the link between science and technology became apparent, governments began to view research as an engine for economic growth and a key factor in achieving international competitiveness. 68 World trade in high-technology products has expanded accordingly; for example, trade in medical and pharmaceutical products grew between 1970 and 1984 from \$2 686 million (current U.S. dollars) to \$14 716 million. 69 The ascendance of the management culture is evident in our government's tendency to set strategic goals for science (for example, the transfer of know-how from the universities to the private sector), to rely on quantitative measures of research performance in evaluating research expenditures, 70 and to devise organizational means to achieve its ends.⁷¹ In industry, the marriage of science and management is evident in the longer-term planning companies do to compete in the high-tech trading world. 72 To take one example, pharmaceutical firms that have traditionally recovered their research and development investment in new products over five to seven years are now thinking in terms of the 10- and 15-year programs needed to build and exploit the basic research capabilities required for molecular biology. So industry is expanding its investment in research73 and aggressively exploiting scientific capability wherever it resides in the world.

Universities, encouraged originally by governments to collaborate with the private sector, now compete with each other for industrial sponsorship and long-term partnerships with companies or groups of companies. As the desire for bankable results gradually replaces the ingenuous search for new knowledge, the values that have traditionally sustained science give way to the managerial mindset. In the long term, science itself may lose

some of its power because of this.74

The managerial perspective on science is not limited to society's attempt to put basic research to work for the economy. Mounting public concern about the environmental and social stresses incurred by industrial

and technological practices has also affected government policy and thus the scientific agenda. In Canada and other affluent countries, the scientific community is repeatedly asked to give its assessment of the dangers posed by this or that development. While governments do not always listen to what the scientists say about environmental damage or technological risk, the fact that their opinions are frequently solicited demonstrates the role they are assumed to play. By deciding how much money to allocate to the different granting councils (and in what proportions) and through initiatives such as the research component of its Green Plan, the federal government in Canada tries to make the scientific community responsive to the concerns and aspirations of society at large.

The Public Perspective

Science permeates contemporary life, yet most people know little about it and understand science culture even less.75 Technology fascinates and repels us at the same time. 76 The popular media tend to depict science when they depict it at all — in either heroic or trivial terms and in a way that inspires ignorance. Despite the occasional detour to celebrate medical breakthroughs or military towrs de force, they generally depict scientists as technocrats.⁷⁷ Only in the biomedical disciplines do scientists avoid unfavourable comparisons with people in the adversarial professions like medicine, law, or sports, where the contest is with disease, the court, or other athletes.

For their part, Jane and John Q Public suffer from low scientific selfesteem. According to a 1986 Harris and Associates survey, only 16 percent of Americans (23 percent of the men and 10 percent of the women) think their basic understanding of science is very good. But they are aware of it as an activity and voice of authority. As an activity, it is involved in the discovery and revelation of truths; as an authority, it is an arbiter of reality, which is to say, if something is scientifically proven it is true. The popular scientist who writes books for children or appears on television to discuss the natural world is the priest displaying the treasures of the temple to the unwashed.

Government broadcasts a different message, however. While budgets for research and development have expanded and expensive advertising campaigns have been deployed recruiting teenagers into the sciences (typically featuring boys on back-to-the-future skateboards sailing over impossibly high-tech landscapes), support for investigator-initiated research has diminished. As the managerial perspective takes in more and more of the science system, as research funding is tailored to meet economic and political objectives, public attitudes toward science are changing. John Durant, a professor at Imperial College in London who specializes in the public understanding of science, has established that most Britons think "the primary aim of science is ... to develop new and useful products."78 Likewise, a survey done by Angus Reid (Winnipeg)

found that three in five Canadians want "more attention paid to industrial

and manufacturing science."79

The public thinks science is man's work. Children "grow up not only expecting scientists to be men, but also perceiving scientists as more 'masculine' than other male professionals, than, for example, those in the arts." Numerous studies confirm that "the 'harder' sciences as well as the 'harder' branches of any profession [are] consistently characterized as more masculine," according to American social scientist Evelyn Fox Keller. Keller cites an English study demonstrating that "scientists are perceived as not only more masculine than are artists, but simultaneously as less sexual." ⁸¹

Most people think science is good for them and have felt that way for a long time. In the United States, there has been a 10-year pattern of gradual growth in the belief that the benefits of science outweigh the risks, for example. A 1987 Harris and Associates poll for the OTA indicated that "the overwhelming majority of the American public (80 percent) expect developments in science and technology in the next twenty years to benefit them and their families."

Canadian attitudes toward science have not been studied as much as American attitudes. However, the available surveys suggest that we are true believers too. Certainly we suspect the country is falling behind in the international science sweepstakes and blame our governments for it. We want more scientific research in many areas, especially the environment, cancer, acquired immunodeficiency syndrome (AIDS), and health research generally. Two-thirds of Canadians questioned by Angus Reid think governments should give more money to cancer research and research on children's diseases. We are evidently less enthusiastic about basic research on the human body or fundamental biology. Expression of the human body or fundamental biology.

The Americans, who drive the international science system by the sheer weight of the billions they spend on research, are even more enthusiastic about science, especially the life sciences. A majority (58 percent) also believes "that unjustified fears of genetic engineering have seriously impeded the development of valuable new drugs and therapies."

The minority who are "anti-science" constitute an interesting group. Women are significant among them, as are racial minorities, the poor, and the less educated, and there is even among them a small subgroup of people who would rather not know at all about some of the things science is discovering. In the 1987 Harris and Associates poll, among those who thought it better not to know various genetic truths, 28 percent were men and 37 percent were women. In general, the people who follow science closely are more likely to be positive about new possibilities like genetic testing. A survey designed by Eleanor Singer of Columbia University indicated that "72.1 percent of those who follow science news very closely, compared with 62.2 percent of those who did not follow it at all, believe the benefits will outweigh the costs."

The Americans, in short, are generally willing to take technological risks to reap the benefits of scientific advance. This is not to say they do

not perceive risk, however; a "dread chart" published by Science in 1987 showed how lack of understanding of a technology contributes to the perception of risk (see Figure 12).⁹¹ Although they do not have much confidence in the ability of government agencies to do the regulating, they do want more social control over science and technology, and they have far more confidence in the academic scientist than in the government expert when it comes to making judgments that concern their well-being.92

While public opinion about emerging technologies such as diagnostics and gene therapy, which are based on molecular biology, has not yet crystallized, there are some indications that people will respond positively. The Singer study and the Harris and Associates polls suggest that genetic technologies will be welcomed, at least in the United States and especially by the male population.

The vast majority of the American public approve of scientists changing the make-up of human cells: to stop children from inheriting a usually fatal genetic disease (84 percent), to cure a usually fatal genetic disease (83 percent), to stop children from inheriting a non-fatal birth defect (77 percent), or to reduce the risk of developing a fatal disease later in life (77 percent).93

The 1987 Harris and Associates report indicates that more than threequarters of Americans would undergo gene therapy to avoid a serious latelife genetic disease, and 86 percent would be willing to have their child undergo genetic therapy, "if the child had a usually fatal genetic disease." 94

In sum, ordinary citizens are alienated from science and technology and feel themselves to be ignorant as well. Most of us are enthusiastic about science and technology all the same, although educated men are more likely to express positive attitudes toward them than are women or the under-privileged in society. There is also that perpetual minority that is resolutely opposed to the continued expansion of the roles of science and technology in modern life. While people seem to agree on the need for increased social control of science and technology, they also feel that scientists themselves are more trustworthy than governments or industry and that governments are poor regulators.

The Critical Perspective

There are serious critiques and queries being raised about science and the new reproductive technologies by scholars, science critics, public policy analysts, feminist researchers, and others who have picked up the warning signals. These people have taken the trouble to think through the implications of science and technology, especially from the point of view of society's most vulnerable citizens — those without power or voice. The instinctive response in many quarters of scientific government/industry establishments has been to dismiss the critics as naysayers and to discount not only their analysis but the alternative perspectives they represent. Yet it is clear to any informed outsider that

their work is intellectually and politically important and is ignored at

everyone's risk.

The critical perspective — the analytic context in which science and technology are evaluated — has at least three major manifestations: the first stems from a criticism that focusses on the dehumanizing effects of science and technology and their potential for devaluing the quality of life; the second is derived from the observation that science no longer determines technology, that the technological tail is wagging the scientific dog; and the third comes from the criticism that science and the scientific system, in interacting with the traditions of the culture, perpetuate the dominance of white, male values.

The Perception of Science and Technology as Dehumanizing

One of the most common criticisms of modern science is that it represents a value system and displays proclivities epitomizing the leftbrain, managerial, and controlling characteristics of human culture. Modern science conceives of nature as object, people as subject, and "man" as the agent-manipulator. Some of the best-known popularizers of science have celebrated the point—for instance, Jacob Bronowski, who asserted in The Ascent of Man that "science looks at nature, takes her apart, and puts her back together in ways which better serve his ends."95 Because science has made possible the invention of certain technologies that have been used to subdue and exploit nature, many people have come to see science as the problem, rejecting the possibility that it might also be part of the solution. Nowhere is such wholesale rejection more likely to occur than in the realm of human reproduction. As William Irwin Thompson has noted. "Pregnancy itself sets up a craving for the old order at the back of time, the order of women's mysteries, the neolithic order of gardening, midwifery, and the medicinal lore of plants."96

Of course, it is not human curiosity that is the culprit but rather the products of the technological imagination. Nobel prize-winning poet Octavio Paz has observed that "technology begins as a negation of the image of the world and ends as an image of the destruction of the world." As an artist, Paz is concerned about our perception of the world around us. As an ordinary citizen, he understands the problem to be one of "adapting technology to human needs rather than the reverse." Others take a more earthy approach: "once a new technology rolls over you, if you're not part of the steam roller, you're part of the road."

Ursula Franklin, long an eloquent critic of the thoughtless application of technology in society, believes that "the temptation to design more or less everything according to prescriptive and broken-up technologies is so strong that it is even applied to those tasks that should be conducted in a holistic way." She argues that such technologies, incorporated into production models that lack links to a larger social and political context, lead to the externalization of considerations, such as the impact of a given

activity on its surroundings. And she worries about society's reliance on production models for applications of the new biotechnologies.

For me the most frightening incursions of production technologies and production thinking have happened in the new human reproductive technologies. The close monitoring of the fetus and some of the invasive prenatal technologies can only be considered as quality-control methods, with the accompanying rejection of substandard products. ¹⁰¹

The Australian sociologist Joanne Finkelstein argues that the biomedical search for correctable human characteristics, and the ideology of human accounting inherent in this search, have been "entirely compatible with the propagation of a technocratic order of society." ¹⁰²

Other critics worry that scientists have short memories. American professors Dorothy Nelkin and Laurence Tancredi are sweeping in their condemnation of scientists who are "oriented only to the present, scientists [who], less than twenty years after the Nazi atrocities, in effect obliterated history." They cite the examples of Linus Pauling's statement that people who have children knowing they risk cystic fibrosis should feel guilty; the 1970 U.S. NAS's Committee on Science and Public Policy statement that "eugenics is a means to expand the human potential to produce a healthier society"; and the call by Bentley Glass, one-time president of the American Association for the Advancement of Science, for "the use of the new biology to assure the quality of all new babies."104 What worries Nelkin and Tancredi is the way the authority of science is used to make a wide range of technological applications credible. One of these is genetic diagnosis. "Normative assumptions about scientific objectivity enhance the power of diagnosis and conceal the values embedded in many tests." Professor Franklin's concern is clearly justified.

For a long time people have understood that science and technology mystify nature. Entering a department store elevator, Virginia Woolf's fictional character Orlando remarks: "The very fabric of life now ... is magic. In the eighteenth century, we knew how everything was done; but here I rise through the air; I listen to voices in America; I see men flying — but how it's done, I can't even begin to wonder." This mystification leads to the devaluation of experience; tradition and common sense cede pride of place in human affairs to expertise. "It is not only perceptions," argues Ruth Macklin, professor of bioethics at Albert Einstein College of Medicine in New York, "but also conceptions of the familiar that become altered by advances in science and technology."

As we have seen earlier, the widespread suspicion that technology drives science is not without grounds; nor is the fear that research decisions are overly influenced by military and industrial demands, which sometimes subvert the process of scientific validation. It used to take a generation before a discovery was integrated into the culture such that it affected people's lives; in our time, the combined demands of industry and, paradoxically, the public who anxiously and expectantly await "answers"

from science have drastically reduced the time span between discovery and innovation, cutting short the validation process. University of British Columbia health care economist Robert Evans complains that the introduction of new medical interventions without compelling proof of their effectiveness in terms of therapy or cost is notorious.

If (some) clinicians find it plausible that a manoeuvre might be beneficial in particular circumstances, it is likely to be used. The growing concern for "technological assessment" or careful evaluation *before* dissemination, is a response to this well-established pattern.¹⁰⁸

As science is turned increasingly to national and corporate interests, the pressure to apply advances in clinical and other market settings intensifies. ¹⁰⁹ As Dr. Evans argues, "those who might wish to restrain application, fearing lack of effect or even harm, find themselves bearing the burden of rigourous proof." ¹¹⁰

While the purpose of patent laws around the world may be, as Abraham Lincoln once said, that of "adding the fuel of interest to the fire of genius," they do not ensure that information about the risks of new technologies will be shared early enough in the innovation process to make a difference. They "may actually promote secrecy in the interest of patent priority," as American sociologist of science Dorothy Nelkin has argued, since "researchers may ... be reluctant to report on their work at meetings or may delay publication until a patent application is filed. 'Patent first, publish later,' is a slogan widely heard as collaborative arrangements between private industry and academia multiply."¹¹¹

The Technology Tail Wags the Science Dog

There is growing awareness that technology is actually setting the scientific research agenda in fundamental ways. The use of computerautomated gene sequencing techniques threatens to turn thousands of biologists into lab technicians and determines the problems that other scientists will address by virtue of the unprecedented flow of data being released. In the United States, "Amoco has invested heavily in a project to sequence a number of bacterial genomes simply because it feels that the software developed for the management and analysis of new data will be commercially valuable."112 Moreover, in new fields such as biotechnology and superconductivity, the push to develop economically viable products and processes is posing technical questions that used to be answered by engineers and managers but that today can be answered only by those working at the frontiers of scientific discovery. An example of this is the field of structural biology, a field where informed observers expect "orders of magnitude of progress ... mainly in how proteins fold, how they function and how they interact to form higher order structures ... Designer proteins are now a dream, but in 10 or 20 years they are likely to be as commonplace as designer blue jeans are today."113

Science and Values

Complementing and exacerbating the anxiety of critics about the way science is translated into everyday technologies is the recognition that some of the so-called tenets of science, including the claim to be "value-neutral," are really statements of intent "designed to ensure the practice of science a niche in society rather than the emancipatory reform of that society." Cornell University philosopher of science Sandra Harding is impatient with those who found their defence of science's objectivity on physics: "Scientific formulas are like legal judgments: the laws become meaningful only through learning (or deciding) how to apply them, and doing so is a process of social interpretation." 115

It is this process that so concerns feminist critics of science. All processes of social interpretation reflect the values of dominant groups. Society is misogynist, and so, therefore, are the interpretations of science. Writes Harding, "sexist science is morally and politically wrong because it supports those desires and interests of men that are satisfied only at the expense of women as a group." 116

The evidence of this prejudice is not hard to find, even in fields that are at a far remove from sex and/or gender. Sexist language abounds in descriptions of fertilization, which is not perhaps surprising; but it is also found in descriptions of the behaviour of obviously asexual chemicals, such as carbene, which gather in molecular clusters around alkene bonds said to be "ripe for plucking." To the examples of sexually aggressive language must be added the frankly dismissive. Consider physicist Richard Feynman's reference in his Nobel lecture to an old and inadequate theory of his as having become an old lady: "but we can say the best we can for any old woman, that she has become a very good mother and has given birth to some very good children." 118

Feminist critics pay a lot of attention to language because language betrays attitude. For example, "the term 'genetic engineering' (like 'reproductive technology') is a masculine metaphor appropriating the role of procreation to technology ... [It] is a science fiction expression suggesting the triumph of phallogocentric lust to recreate the world without the intermediary of fleshy women's bodies."¹¹⁹

Then, too, the division of labour in science is consistent with the division of labour in the larger society. A study conducted by the National Science Foundation in Washington established that, in 1985, 87 percent of applicants for the agency's research grants were men, 89 percent were white, 9 percent were Asian, and 2 percent were members of other racial/ethnic groups. 120 Women were disproportionately represented in the one-time recipient category and under-represented in the consistent award category. Successful candidates in this latter category were "more likely than the average applicant to be male, older ... and much more likely to be associated with a 'top 21' institution. Ninety-seven percent had served as a reviewer or panellist." The Royal Society of Canada has documented the representation of women among its own fellows, as well as in other

academies; the numbers are depressing. In 1989, 5 percent of the Society's fellows, including fellows in the academies that represent the humanities and social sciences, were women. Approximately 3.1 percent of the members of the Royal Society of London are women. The NAS in the United States does slightly better, at 3.4 percent, while in Sweden women make up only 1.7 percent of the members of the Academy of Science. 122

Not only are women under-represented in science, but activities that have traditionally been thought of as female activities have been excluded from the purview of science. Ruth Ginzberg suspects that "gynocentric science often has been called 'art,' as in the *art* of midwifery, or the *art* of cooking, or the *art* of homemaking. Had these 'arts' been androcentric activities, I have no doubt that they would have been called, respectively obstetrical *science*, food *science*, and family *social science*. Indeed as men have taken an interest in these subjects they have been renamed sciences — and, more importantly, they have been reconceived in the androcentric model of science." Not surprisingly, then, the focus of the most radical of the challenges to science is the "conjunction of science's role in the social construction of gender and sexuality with a masculine-dominant social order's role in legitimating scientific authority for the purpose of increased social power." 124

Some critics have demonstrated that the research agenda reflects women's powerlessness in science. One often-cited example is the fact that only 13.5 percent of the budget of the NIH (in 1987) was for research on female health issues. ¹²⁵ Informed observers have long complained about the low level of the agency's spending on breast cancer, a leading cause of death among women, for example. ¹²⁶ The limited spending on reproductive health research likely reflects this bias as well.

What many scientists do not seem to understand about feminism is that the movement has an all-inclusive social agenda within which the critique of science must be situated. Sandra Harding asks, "Must not feminism take on as a central project of its own the struggle to eliminate class society and racism, homophobia and imperialism, in order to eliminate the sexist uses of science?" 127

It is important to remember that the sexist agenda is assumed and unconscious while the feminist agenda is posited and conscious. This is one of the reasons why the women's movement can be expected to be suspicious of scientific and technological advances that have particular applications to the female sex. Appeals to the idea that science is an objective undertaking simply do not respond to the concerns of feminist critics of the new reproductive technologies.

Conclusion

Evidently, ours is a culture that sets great store in science. For the most part, the general public believes in its virtues and the value of the technologies it spawns; industry and government expend vast energies in the effort to harness its power to the national and corporate purpose. Within the archly competitive research environment, investigators struggle to secure funding to continue their work, keeping one foot in the academic world and the other in trade and commerce. University-based scientists, especially molecular biologists, have come to realize that the opportunities for sponsorship (and personal financial reward) lie in joining or creating new companies. This suits larger and long-established firms, especially the pharmaceutical companies, just fine; they bide their time until it makes sense for them to buy into the new ventures or develop the innovative products created by them. As the gap between technology and basic science narrows, sponsors put more emphasis on intellectual property rights.

The practice of medicine — which many ordinary people think of as being scientific, but which scientists think of as pretty much of a hit-and-miss affair, for all its stainless steel trappings — is being transformed by the application of enabling technologies such as computers and molecular biology. The latter, in particular, is developing new and far-reaching powers to prevent, diagnose, and treat disease. Distinctions between the life sciences and technologies of research are proving more difficult to define, especially in the emerging field of biotechnology, which is already producing remedies for once incurable pathologies and which will certainly have profound impacts on reproduction.

There are, in other words, powerful forces pushing for the rapid development and application of science and technology, including reproductive technology, that are driving science to push itself to accelerate the process of discovery. At the moment, the only restraints in sight are the finite store of resources and the willingness of society to make sacrifices in other areas in favour of science and technology — and regulations.

While the regulatory framework for the commercialization of health care products is well established, that for scientific research is in a state of flux. Regulations affecting research on human reproduction in industrialized countries range from informal guidelines to legislated and enforced rules. In Canada, as elsewhere, the scientific community prefers to regulate itself.

Reproduction — A Field of Only Limited Interest to Researchers and Industry

Pressure to "make it" in the scientific community is intense. Scientists learn to strategize early in their careers to find subjects with potential for major discovery and international recognition. The usual tactic is to search

out domains with unanswered fundamental research questions, with access to adequate funding, and (ideally) without restrictions on avenues of research. In this regard, human reproduction is not a competitive field of research — funds are in short supply, regulations abound, and the issues raised by research are so socially and morally significant that to mention them is almost to generate public controversy.

Meanwhile, industry's mission is to survive and grow in the competitive commercial environment. To do this, companies have to capture and commercialize useful technological advances. Molecular biology, including its applications to human reproductive biology, is one of the most important of these areas; advances in medicine, forestry, and agriculture, among others, all originate with progress in the life sciences. However, as far as business opportunities are concerned, human reproduction offers little more than a few niche products with limited commercial potential. The ethical, cultural, and political terrain surrounding the technologies of human reproduction does not endear the field to investors or attract support in the development and commercialization of products and services.

The Role of Government — Balancing Public and Private Interests

It is to governments that the task of balancing public and private interests is entrusted by society. As promoters of knowledge-based industry, governments set up programs and incentives to develop and attract high-technology industry and the qualified scientific personnel and infrastructure on which this industry depends. As regulators, their aim is to establish conditions for industrial development and scientific research that protect the public.

Public opinion in the United States and Canada tends to support the notion of science as an engine of economic and social development and is especially supportive of research that relates to human health. However, there are significant minorities who are critical of unrestrained scientific advance and technological development. There is also a significant body of informed critical thought that challenges many of the assumptions and methodologies as well as the organization and staffing of modern science. Some people are calling for moratoria on some kinds of research and strict regulation of others.

However, moratoria are not likely to work in a global science system, unless the research community itself imposes the ban. Moreover, regulatory mechanisms can have unintended side-effects, such as prompting a "rationalization" of an industry so that a few relatively large companies or institutions dominate a sector and exercise untoward influence on public policy overall. The threat of restrictive measures also tends to make the organized scientific community defensive about its mission and less willing than it would be otherwise to flag problems of its own accord.

Highly restrictive regulations can also have unanticipated negative effects. The following assessment of the effect of the American moratorium on the funding of some kinds of research on human reproduction is illustrative.

The effect of this moratorium on Federal funding of IVF research has been to eliminate the most direct line of authority by which the Federal Government can influence the development of both embryo research and infertility treatment so as to avoid unacceptable practices or inappropriate uses. It has also dramatically affected the financing ability of American researchers to pursue improvements in IVF and the development of new infertility treatments, possibly affecting in turn the development of new contraceptives based on improved understanding of the process of fertilization. 129

The NIH has estimated that it would receive more than 100 applications annually for grants to do research on human IVF if the moratorium were not in place. 130

Ironically, restrictive regulations may simply encourage scientists to move to jurisdictions where they can pursue their research more freely. ¹³¹ The American moratorium on funding for some kinds of investigations in the field of human reproduction has not stopped the research. Funding for research on human IVF in the United States today comes from the private sector and from the operating budgets of universities and medical centres. These are outside federal control.

A further consideration is the problem of regulations becoming a barrier to investment in a jurisdiction that is trying to create or market its cluster of research programs and infrastructure. When this happens, two levels of public policy conflict, and one or another public interest must be sacrificed.

The Scientific Community — A Partner in Social Responsibility

The scientific community is a resource on which Canadians can call to play an expanded, proactive role in the identification and management of the risks attached to scientific advance. The "scientization" of medicine and a host of other fields raises profound questions about the nature of human responsibility toward self, society, and the biosphere. Scientists are well placed to predict and describe this process.

This begs the need for improvement in the ways the scientific community communicates with the governments that ultimately control the pace and scope of technological development and that must balance the roles of promoter and regulator. And it further raises the problem of scientists communicating with the public, whose views about science tend toward polarization and stereotyping. Changing this situation — as Nobel laureate John Polanyi for one has persistently argued — means the scientific community has to participate in public debate. It is not public relations that is needed, but engagement with the issues of the day.

Limitations of the Scientific Community — The Need for Change

Scientists like to describe their community as a craft guild, a society of peers with collective (if not always individual) loyalty to long-standing principles of investigation and verification. The reality is often different. Individual scientists can and do check their prejudices at the lab door, but science as a whole serves a culture that does not celebrate the naive mind. It is oriented toward productivity and performance — whether that performance bears on the generation of wealth or the amelioration of problems. It looks to the future, and its language is managerial, defining populations as targets, forests as resources, and citizens as consumers.

Recommendations

The principal lessons of this review of the science and technology system and the ways in which the system is perceived by the various "stakeholders" can be summarized as follows:

- 1. The system is global, and unilateral attempts to control any one part will have to take that into account.
- 2. The active cooperation and collaboration of the science community are essential to effective social control of the development and implementation of the new technologies.
- 3. The ability of the scientific community to play a proactive role in the identification and management of risk is compromised by the inequities of its own structures and culture, society's alienation from the community, and the erosion of the community's traditional values as it relies increasingly on the external sponsorship of research in a highly competitive environment.

In developing its recommendations, the Commission may wish to address the following issues:

- 1. the effects on the development and use of new reproductive technologies of measures that would constrain research and testing in Canada;
- 2. the potential of existing scientific institutions and organizations in Canada to establish, mandate, and manage "watchdog" review committees and permanent commissions, which would ensure, first, that socially or morally significant research advances that concern or could concern the reproductive process are adequately understood by the scientific community at large, policy makers, and the general public; and, second, that the research practices of scientists in Canada are effectively scrutinized by their peers; and
- the need for the scientific community in Canada to consider and respond to, in the context of reproductive biology and technology,

the critiques of its values and performance that have been advanced by scholars and social activists.

Figure 1. Recipients of Medical Research Council Grants for Reproduction Research (1991)

Name	Affiliation	Area of research
Armstrong, D.T.	Dept. of Obstetrics and Gynaecology University of Western Ontario	Ovary Steroid Gonadotropin
Baines, M.G.	Dept. of Microbiology and Immunology McGill University	Immunology of Fetus Spontaneous Abortion
Belisle, S.	Département d'obstétrique- gynécologie Université de Montréal	Aging, Gonadotropins, Steroid Receptors
Belisle, S.	Département d'obstétrique- gynécologie Université de Montréal	Chorion Gonadotropin Pregnancy
Bose, R.D.	Dept. of Obstetrics, Gynaecology and Reproductive Sciences University of Manitoba	Embryo Associated Immunosuppression Immunoassay
Brawer, J.R.	Dept. of Anatomy McGill University	Polycystic Ovaries, Anovulation, Neuroendocrinology
Bureau, M.A.	Faculté de médecine Centre hospitalier universitaire de Sherbrooke	Newborn Breathing Disorders
Carnegie, J.A.	Dept. of Obstetrics and Gynaecology Ottawa Civic Hospital	Extracellular Matrix, Reichert's Membrane, Parietal Endodermal Cell Migration, Endocrinology
Casper, R.F.	Dept. of Obstetrics and Gynaecology Toronto General Hospital	Menopause, Hormone Replacement Therapy
Clark, D.A.	Dept. of Medicine McMaster University	Pregnancy Suppressor Cells
Clarke, H.J.	Royal Victoria Hospital McGill University	Oocyte Maturation, Embryo

Figure 1. (cont'd)	Figure	1.	(cont'd)	
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Figure 1. (cont'd)		
Name	Affiliation	Area of research
Clermont, Y.W.	Dept. of Anatomy McGill University	Testis Spermatogenesis
Crankshaw, D.J.	Dept. of Obstetrics & Gynaecology McMaster University	Birth Oxytocin
Dorrington, J.H.	Banting and Best, Dept. of Medical Research University of Toronto	Ovary Follicular Development
Evans, J.A.	Dept. of Human Genetics University of Manitoba	Birth Defects Taxonomy
Faiman, C.	Section of Endocrinology & Metabolism Health Sciences Centre, Winnipeg	Non-Human Pituitary Gonadotropins
Faucher, D.J.	Royal Victoria Hospital McGill University	Intrauterine Adaptation, Perinatal Neuroendocrinology, Hypoxemia, Vasopressin, Corticotropin, Stress
Fraser, W.D.	Département de périnatologie Hôpital Saint-François d'Assise	Dystocia Amniotomy
Fraser, W.D.	Département de périnatologie Hôpital Saint-François d'Assise	Repeat Caesarian Section Vaginal Birth After Caesarian Section
Fritz, I.B.	Banting and Best, Dept. of Medical Research University of Toronto	Spermatogenesis Sertoli Cells
Gagnan-Brunette, M.	Centre de recherche Hôpital Maisonneuve-Rosemont	Placenta Calcium Phosphate Transport
Gagnon, C.	Urology Research Laboratory Royal Victoria Hospital	Spermatozoa, Motility of
Gagnon, C.	Urology Research Laboratory Royal Victoria Hospital	Spermatozoa, Sperm Separation

Figure 1. (c	ont'd)
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Name	Affiliation	Area of research
Gagnon, R.	Lawson Research Institute St. Joseph's Health Centre	Fetal Heart, Cardiac Doppler Flow, Assessment of Fetal Health
Garfield, R.E.	Dept. of Biomedical Sciences McMaster University	Pregnancy, Birth
Gibb, W.	Dept. of Obstetrics and Gynaecology University of Ottawa	Birth Prostaglandins
Greenblatt, E.M.	Dept. of Obstetrics & Gynaecology Toronto General Hospital	Corticotropin-Releasing Factor, Ovary, Stress Reproduction
Hales, B.F.	Dept. of Pharmacology and Therapeutics McGill University	Cyclophosphamide Male Germ Cell
Hannah, M.E.	Dept. of Obstetrics and Gynaecology Women's College Hospital	Induction of Labour, Clinical Trial
Hannah, M.E.	Dept. of Obstetrics and Gynaecology Women's College Hospital	Pregnancy, Birth, Induction
Harding, P.G.R.	Dept. of Obstetrics and Gynaecology St. Joseph's Health Centre	Surfactant, Indomethacin, Cerebral Blood Flow, Newborn Intraventricular Haemorrhage, Newborn Handi
Jacobson, W.	Division of Reproductive Sciences Toronto General Hospital	Puberty Gonadotropin Release
Jones, S.A.	Samuel Lunenfeld Research Institute Mount Sinai Hospital	Placenta, Parturition, Preterm Labour, Prostaglandins, Corticotropin-Releasing Hormone
Kalousek, D.K.	Dept. of Cytogenetics and Embryopathology B.C. Children's Hospital	Chromosome Mosaicism Fetus

Figure	1.	(cont'd)
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Name	Affiliation	Area of research
Kan, F.W.K.	Département d'anatomie University of Montreal	Fertilization, Spermatozoa
Khalil, M.W.	Dept. of Obstetrics and Gynaecology University of Western Ontario	Ovary Granulosa 19- Norsteroids
Kidder, G.M.	Dept. of Zoology University of Western Ontario	Blastocyst, Gene Expression, Na-K-ATPase Sodium Transport
Koren, G.	Dept. of Paediatrics and Pharmacology The Hospital for Sick Children, Toronto	Placenta Calcium
Lala, P.K.	Dept. of Anatomy University of Western Ontario	Fetomaternal Interface, Spontaneous Abortion
Laskin, C.A.	Toronto General Hospital	Pregnancy, Miscarriage, Aspirin, Prednisone
Leung, P.C.K.	Dept. of Obstetrics and Gynaecology University of British Columbia	Gonadotropin-Releasing Hormone, Ovary, Steroidogenesis
Librach, C.L.	Dept. of Obstetrics and Gynaecology University of Toronto	Pregnancy, Placenta, Trophoblast, HLA-G, Histocompatibility
Manjunath, P.	Centre de recherche Hôpital Maisonneuve-Rosemont	Gonads, Regulatory Peptides
Martin, R.H.	Medical Genetics Clinic Alberta Children's Hospital	Sperm Chromosome Abnormality
Mitchell, B.F.	Dept. of Obstetrics and Gynaecology University of Alberta	Fetus Estrogen
Morrish, D.W.	Dept. of Medicine University of Alberta	Growth Factors, Placenta
Moutquin, JM.	Centre de recherche Département d'obstétrique et de gynécologie Hôpital St-François d'Assise	Pregnancy Pre-Eclampsia

Figure 1. (cont'd)

Name	Affiliation	Area of research
Murphy, B.D.	Dept. of Obstetrics and Gynaecology Royal University Hospital, Saskatoon	Corpus Luteum Progesterone, Cholesterol
Pattinson, H.A.	Dept. of Obstetrics and Gynaecology University of Calgary	Sperm Count
Pomerantz, D.K.	Dept. of Physiology University of Western Ontario	Testis Leydig Cells
Rajabi, M.R.	Dept. of Obstetrics and Gynaecology Royal Victoria Hospital	Birth, Cervical Dilatation at Parturition, Hormonal Regulation of Collagenase
Reid, R.L.	Division of Reproductive Endocrinology Queen's University	Endometrial Ablation, Photodynamic Therapy
Robaire, B.	Dept. of Pharmacology and Therapeutics McGill University	Epididymis, Steroids, 5- alpha-Reductase, Glutathione S- Transferases, Cadherins, Immobilin
Rossant, J.	Samuel Lunenfeld Research Institute Mount Sinai Hospital	Trophoblast Gene Expression
Russell, A.S.	Dept. of Medicine University of Alberta	Rheumatoid Arthritis, Pregnancy, Collagen, Arthritis
Sairam, M.R.	Reproduction Research Laboratory Clinical Research Institute of Montreal	Contraception, Fertility, Ovary, Testis
Schultz, G.A.	Dept. of Medical Biochemistry University of Calgary	Fertilization, Gene Expression
Sullivan, R.	Centre de recherche Hôpital Maisonneuve-Rosemont	Spermatozoids, Epididymis

Figure	1.	(cont'd)
		()

Name	Affiliation	Area of research
Taketo-Hosotani, T.	Urology Research Laboratory Royal Victoria Hospital	Infertility, Oocyte Maturation, XY Ovary, Aromatase
Taketo-Hosotani, T.	Urology Research Laboratory Royal Victoria Hospital	Gonadal Sex Reversal, Vascularization
Tanphaichitr, N.	Dept. of Obstetrics and Gynaecology Ottawa Civic Hospital	Spermatogenesis, Fertilization
Trasler, J.M.	Research Institute Montreal Children's Hospital	Spermatogenesis, DNA- methylation, Gene Expression in Mice
Varma, D.R.	Dept. of Pharmacology & Therapeutics McGill University	Fetal Toxicology, Methyl Isocyanate, Utero Placental Bloodflow, Stillbirth, Bhopal Catastrophe
Vogl, A.W.	Dept. of Anatomy University of British Columbia	Spermatozoa Actin
Wells, P.G.	Faculty of Pharmacy University of Toronto	Chemical Teratogenesis, Embryo, Cell Culture, Fetus
Zalik, S.E.	Dept. of Zoology University of Alberta	Embryo Cell Differentiation

Source: Medical Research Council; extract from the data base.

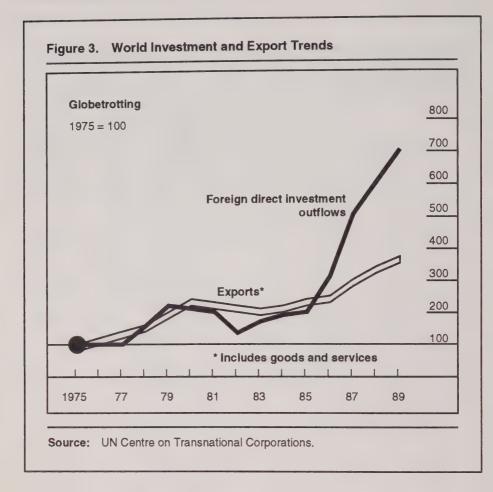
Figure 2. International Comparisons (1987) of Government Expenditures on Health Care Research and Development in Canada and Selected Other Countries

	GERD (US \$ million)	GERD/GDP (%)	R&D share financed by gov'ts (%)	Health care R&D share of gov't- financed R&D (%)	Health care R&D financed by gov't (US \$ million)	Gov't- financed health care R&D / GDP (%)
Canada	6 200	1.40	45.8	7.9	224	0.050
France	16 200	2.27	52.9	3.6	308	0.043
F.R.G.	22 900	2.81	33.6	3.2	246	0.032
Japan	46 100	2.87	21.7	2.4	240	0.015
U.K.	15 500	2.36	38.9	4.3	259	0.039
U.S.A.	120 300	2.69	50.9	11.9	7 271	0.163

GERD = Government Expenditures on Research and Development

GDP = Gross Domestic Product R&D = Research and Development

Source: NGL Consulting Ltd.



Research	
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Figure 4.	

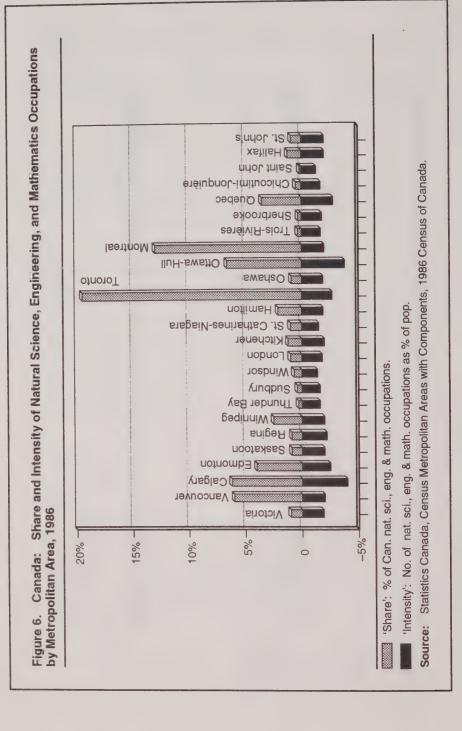
	Acceptance of classified research	Acceptance of publication delays	Acceptance of proprietary information	Acceptance of pre-publication review by sponsor	Acceptance of restricting publication of results	Mandatory disclosure of purpose, scope, sponsor, etc.
Harvard	no	no "significant" delay	по	yes	no	yes, but no proposal text
Yale	no, nor any "secret" research	(NR)	(NR)	no, except with special approval	no, except with special approval	(NR)
Columbia	no	no "unreasonable" delay	no	(NR)	по	(NR)
TIW	no, not on campus (NR) without special OK (Lincoln Lab excluded)	(NR)	(NR)	(NR)	00	yes, except with prior approval
University of no, v	with possible	(NR)	(NR)	(NR)	"normally not acceptable"	(NR)
Johns Hopkins		(NR)	yes, but negotiated (NR) through the individual	(NR)	"generally unacceptable"	yes, except in national emergency
Princeton	00	30 days with yes, but possible extension discouraged to 90 days		yes	Ou	(NR)

	Acceptance of classified research	Acceptance of publication delays	Acceptance of proprietary information	Acceptance of pre-publication review by sponsor	Acceptance of restricting publication of results	Mandatory disclosure of purpose, scope, sponsor, etc.
University of no Pennsylvania	no	3 months	no, with exceptions	(NR)	no, except to protect privacy of individual	yes, with exceptions
Cal Tech	no, except with President's OK	(NR)	(NR)	(NR)	(NR)	(NR)
Stanford	no, with exceptions possible for access	90 days	yes, with conditions	yes	OL C	yes, except to protect individual privacy
University of	University of selective (NR) Illinois acceptance if compatible with educational and intellectual purposes of university	(NR)	(NR)	(NR)	yes	, ves

NR = No Response

Source: U.S. Institute of Medicine, Government and Industry Collaboration in Biomedical Research and Education, Report of a Workshop (1989).





Chemical and biological biological search Preclinical trials, compounds show safety and tested Clinical trials, compounds show safety and strate canding and promise efficacy trials are biochemically at continues. Clinical trials, clinical trials, clinical trials, comparative tests again in the same of the compounds show safety and synthesized, and show safety and synthesized, and study, a process 50 volunteers. Clinical trials, phase II Acceptance phase IV Acceptance phase IV Acceptance phase IV From any 10 000 Twenty Ten make it to preparations that compounds show safety and sare biochemically to go into further with a healthy to go into further with a healthy to go into further with a healthy tested Virtue on the compounds show safety and synthesized, and shurmacological group of 20 to patients that continues at the compounds illnesses. Only are intended to one out of the page and trials, is analyzed market. All the information phase IV Acceptance phase IV Acceptance phase IV Acceptance All the information of the phase III Acceptance All the information phase IV Acceptance phase IV Acceptance phase IV Acceptance All the information of the phase III Acceptance All the information phase IV Acceptance phase IV All the information of the phase III Acceptance All the information of the phase III Acceptance Acceptance phase IV All the inform	rigure 7. The Drug Development Process in Canada	orug Developm	ent Process In	Canada			
Preclinical Clinical trials, Clinical trials, development phase I phase II y 10 000 Twenty Ten make it to Five pass into compounds show safety and extensive trials nemically sufficient promise efficacy trials with 50 to 100 to go into further with a healthy volunteer pharmacological group of 20 to patients study, a process 50 volunteers. Ithe illnesses until approval for market.	0 (years) 1	2 3				11 12 13	
y 10 000 Twenty Ten make it to Five pass into compounds show safety and extensive trials nemically sufficient promise efficacy trials with 50 to 100 to go into further with a healthy volunteer pharmacological group of 20 to patients study, a process 50 volunteers. suffering from that continues until approval for market.	Chemical and biological research	Preclinical development	Clinical trials, phase I	Clinical trials, phase II	Clinical trials, phase III	Acceptance	Introduction, phase IV
	From any 10 000 oreparations that are biochemically researched, synthesized, and tested	Twenty compounds sho sufficient promis to go into further pharmacological study, a process that continues until approval for market.	Ten make it to w safety and e efficacy trials r with a healthy group of 20 to 50 volunteers.		Two go on to comparative tests with conventional therapies on 500 to 5 000 volunteer patients with the same illnesses. Only one out of the original 10 000 proves its worth as an innovative therapy.	All the information gathered by the company, including chemical structure, results of the studies and trials, and production details, is analyzed by Health and Welfare Canada.	The company disseminates material to health professionals based on government reviews prescribing information.

	Introduction, phase IV	The company is responsible for monitoring patterns of use and effectiveness of the new therapy.	Effective patent life for return on investment (7 to 10 years).
11 12 13	ceptance	New Drug Submission (NDS) by company reviewed by Health and Welfare Canada, and Notice of Compliance (NOC) issued (one to three years).	continues
9 10	Clinical trials,	Review of data by Health and Welfare Canada.	Patent granted but development continues
7	Clinical trials, Clinical trials, phase II phase II	Review of data Review of data by Health and by Health and Welfare Canada.	Patent granted I
5 6	Clinical trials,	Investigating New Drug Submission (INDS) filed with Health and Welfare Canada prior to human trials.	nding (two to s).
2 3	Slinical	REGULATORY: Investigating New Drug Submission (INDS) filed with Health a Welfare Can prior to huma trials.	PATENT: Patent pending (two to three years).
Figure 7. (conf'd)	Chemical and biological research		7d

Source: Pharmaceutical Manufacturers Association of Canada.

Diary of a Drug Figure 8.

It took Merck almost 40 years to bring its cholesterol drug lovastatin to market

Early 1950s Research begins into the formation of cholesterol 956-57 Scientists at Rahway, N.J.-based Merck & Co. isolate mevalonic acid and be converted into cholesterol demonstrate that it can

oxygenated sterols to slow the enzyme 973 Unsuccessful attempts to use that helps create cholesterol February, 1979 Isolation of the enzyme inhibitor lovastatin June, 1979 Merck files for a U.S. patent on lovastatin

August, 1979 Testing of lovastatin on animals begins

April, 1980 Clinical trials begin

clinical trials because of rumours that a compound closely related to lovastatin September, 1980 Merck discontinues may cause cancer in dogs

July, 1982 Doctors arrange with U.S. Food and Drug Administration to use lovastatin disorders. Success with few side effects to treat patients with severe cholesterol

August, 1982 Testing on animals resumes

May, 1984 Beginning of long-term toxicology on high-risk coronary patients. Drug is studies on dogs and clinical trials well tolerated

October, 1986 Animal studies show no tumours in dogs

patients with high cholesterol that cannot November 1986 Filing of 160-volume August, 1987 FDA approves drug for New Drug Application to FDA

June, 1988 Canada's Health Protection Branch approves lovastatin in Canada

be reduced by dieting

A. Walmsley, "Pill Hill North," Report on Business (October 1991), 46. Source:

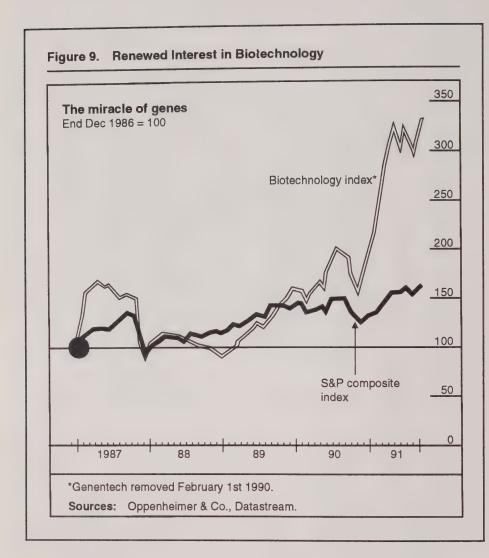


Figure 10.	Figure 10. Regulation Regarding NRT Research in Selected Countries
Country	Comments
Australia	 The State of Victoria Infertility Act bans the production of embryos solely for research and allows research on surplus embryos (for 14 days) only in the experiments approved by a review committee. (The State of South Australia has also passed similar legislation.) The National Health and Medical Research Council has issued guidelines on human experimentation. Research on embryos is acceptable up to the stage at which implantation would normally occur, providing the experiment is approved by an institutional review committee.
Canada	 The Medical Research Council has issued guidelines on human experimentation. Research on human embryos is acceptable up to 14 to 17 days providing research proposals are approved by local research ethics board. There is opposition to the creation of embryos for research purposes.
Germany	 Scientific Council of the German Medical Association issued guidelines on professional standards on IVF and embryo research. The Benda Report (1985) produced by the Federal Ministries of Research and Technology and of Justice recommended restrictions on non-coital reproduction techniques (e.g., creation of embryos not acceptable). Restrictive legislation has been drafted.
France	 Comité Consultatif National d'Éthique (CCNE), which has no legal authority, published reports on NRT issues. CCNE recommended that research on human embryos be acceptable up to seven days.
Sweden	 Government established (in 1982) the Committee on Genetic Integrity to study issues arising from the use of generic engineering. Committee did not propose limits on human embryo experimentation but suggested ethical norms (e.g., 14-day limit on human embryo experimentation).

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Country	Comments
Jnited	• The Warnock Committee (1984) recommended that a statutory licensing authority be established to regulate
Kingdom	certain infertility services and related research.
)	• In response, Medical Research Council and the Royal College of Obstetricians and Gynaecologists formed a
	Voluntary Licensing Authority (VLA). (Legislation has been introduced to make the VLA a statutory body.)
	 VLA quidelines allow research on embryos up to 14 days with the consent of both donors.

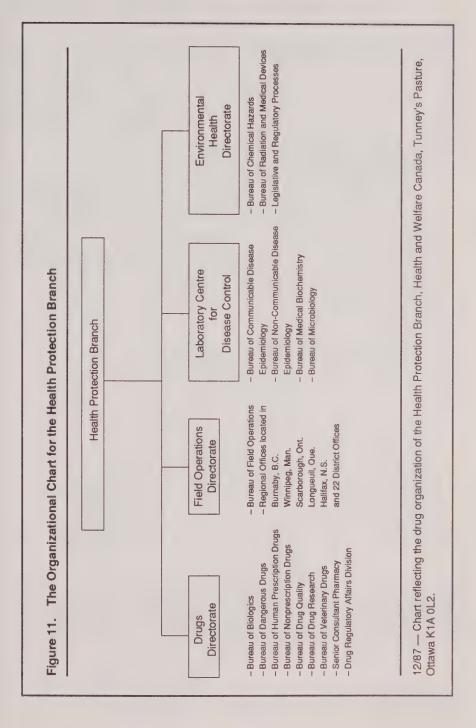
 National Research Award Act (1974) established the National Commission for the Protection of Human Subjects of Biomedical and Behaviourial Research, which sets down regulations for federally funded research United States

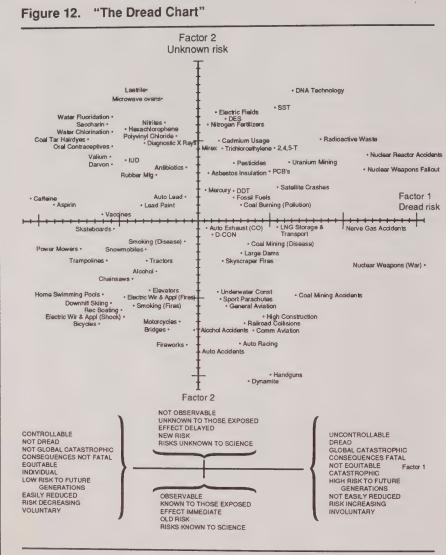
Research is to be reviewed by local review group

An Ethical Advisory Board (EAB) was established to advise on the acceptability of research proposals from an ethical standpoint; however, in 1980 the EAB was disbanded, placing an unofficial moratorium on all federal funding of IVF research.

States' statutes have also placed restrictions on fetal research.

Source: U.S. Congress, Office of Technology Assessment, Infertility: Medical and Social Choices (Washington, DC: U.S. Government Printing Office, 1988).





Note: Location of 81 hazards on factors 1 and 2 derived from the relationships among 18 risk characteristics. Each factor is made up of a combination of characteristics, as indicated by the lower diagram.

Source: P. Slovic, "Perception of Risk," Science 236 (1987), 282.

Appendix 1. Guidelines for Medical Research

(Summarized from the Medical Research Council [MRC] brief to the Royal Commission on New Reproductive Technologies, April 1991)

Research with Embryos

The MRC Guidelines on Research Involving Human Subjects (pages 34-35) state the following:

The Committee views embryo research as an evolving area where Canada does not have a social consensus and where individual values are strongly held, but also evolving. Although there is an opportunity for abuse in the use of *in vitro* fertilization in embryo research, as in the application of any technology, the Committee sees a broad prohibition of all research on embryos as neither justified nor wise. Decisions on the details of research proposals involving embryos will vary with regional and individual differences, and thus the local REB [Research Ethics Board] is an appropriate forum in which to assess each protocol. In reaching its decision, an REB must take into account the embryo as human life at an early stage of the life cycle and the purpose for which the research is proposed. Wherever reasonably possible, such research should be undertaken instead with non-human life forms, or with tissues from abortuses.

At this time, the Committee believes that the purpose of intended research is a critical element in deciding whether embryo research is acceptable. In the Committee's view, it is not acceptable at this point to create embryos in vitro for research as opposed to therapeutic purposes. The Committee believes that for now such research should be limited to research directed toward improvement of infertility management, using embryos up to a stage of development of no more than 14 to 17 days. Research designed to establish the safety and effectiveness of procedures such as in vitro fertilization may especially merit consideration. In time, with the evolution of social and ethical values and further scientific development, REBs and investigators might contemplate other embryo research for such purposes, for example, as genetic correction.

(Note: MRC has endorsed the opinions of the Committee that drafted the Guidelines)

In the Guidelines, as with comparable statements from other countries, the time period of 14 to 17 days was chosen because it corresponds to the time of formation of the primitive streak, and to the stage of development when the cells of the embryo have become specialized to the extent that formation of identical twins is no longer possible.

Research Using Fetal Tissue

The wide availability of fetal tissues resulting from therapeutic termination of pregnancies greatly extends our ability to study the regula-

tion of gene expression and the controls over growth and development

during fetal life.

Studies of fetal cells or tissues *in vitro* are essential to further knowledge of the controls of fetal growth, maturation, and development and can be expected to lead to continuing efforts to promote intrauterine maturation in infants for whom preterm delivery is threatened. Such studies might also lead to a better understanding of fetal growth and of the responses of the developing fetus to adverse intrauterine situations, including hypoxaemia and hypoglycaemia.

The possibility has also arisen that implantation of fetal cells into patients might offer new therapeutic methods for treatment of diseases, such as Parkinson's or diabetes. Research into these techniques is now under way in the United States, Sweden, and the United Kingdom, and a Canadian centre has recently obtained approval through appropriate ethical review. The results of these trials have not yet been published in a form

that permits scientific analysis.

The MRC's Guidelines on Research Involving Human Subjects accept the use of tissues or cells obtained from elective abortions in research designed to improve understanding of health and disease or to provide means of treating intractable disease; however, at least three conditions must be met:

- 1. Research requirements must exert no influence on any aspect of the abortion, including the decision to abort, the timing, and the procedures used.
- 2. Consent of the mother to use the tissues or cells must be obtained.
- 3. The research protocol must be approved by a REB as outlined in the Guidelines.

Somatic Cell Gene Therapy in Humans

The first trials of somatic cell gene therapy have now been carried out in the United States. As anticipated, the first trial has involved young children suffering from a rare and inevitably fatal immunodeficiency disorder caused by a defect in a single identified gene carried by both parents. Other candidates for somatic cell gene therapy are also being studied intensively, and it is anticipated that applications will soon be made for research involving somatic cell gene therapy in Canada.

The MRC's Guidelines on Somatic Cell Gene Therapy in Humans (p. 41) come to the following conclusions:

1. The rapid growth of knowledge in human genetics in Canada and in other countries is now leading to proposals to undertake research in somatic cell gene therapy to attempt to treat some

inherited disorders that cause devastating and presently untreatable disease and early death.

- 2. For the foreseeable future, research in humans on gene therapy should be considered only for diseases which meet all the following criteria:
 - they are caused by a defect in a single gene
 - they cause a liveborn human being to suffer severe debilitation or early death
 - they cannot be treated successfully by any other means.
- 3. For the foreseeable future, there should be no attempts to undertake research in humans which involves deliberate alteration of the patient's germ line, or which involves gene transfer in human embryos.
- 4. Research with animals and with other models in the area of somatic cell gene therapy for humans is needed and appropriate.
- 5. Any attempt to treat an inherited disease by somatic cell gene therapy should be regarded as a research protocol, and subject to procedures and considerations as outlined in this document and in the MRC's *Guidelines on Research Involving Human Subjects*.
- 6. A National Review Committee should be formed to evaluate all proposals in Canada for research on somatic cell gene therapy in humans. A prerequisite for submitting protocols to the National Review Committee is that they should first have been accepted by their local Research Ethics Board.

Present techniques for insertion of DNA sequences require large numbers of cells or embryos and selection of the one or two cases that "work" out of the many that do not.

While potentially precise enough for somatic cell gene therapy, these techniques are not nearly precise enough to insert a sequence accurately and reliably into the correct site of the appropriate chromosome and hence are not acceptable for "therapeutic" methods on human embryos.

Controls over Research

The MRC uses public funds to support research required for full understanding of a very wide range of human disease.

The peer review process by which MRC decides on what research to fund is exacting. Applications are reviewed in competition with each other for the limited funds available. The over-riding priority is the excellence of the science proposed and its relevance to human health. Evaluation of scientific excellence requires consideration of the relevance and design of the research proposed, the importance of the questions being addressed, and the scientific contributions and training of the applicants. The applications are evaluated by peer review committees of leading Canadians scientists; these committees are advised by external referees, many from

other countries, who are selected for their expertise in the area of the

research proposed.

A careful process for ethical review of research is set out in the MRC Guidelines on Research Involving Human Subjects. Very briefly, a REB must be established under the authority of the president or principal of the university or comparable chief executive officer of a non-university institution. The REB must review each research protocol before the first potential subject is approached and has the authority to approve the research, to refuse to allow it to proceed, or to require changes to the protocol for reasons of ethics.

Notes

- 1. U. Franklin, The Real World of Technology (Toronto: CBC Enterprises, 1990), 15.
- 2. Ibid., 11.
- 3. According to American studies cited in a speech given by Commission chairperson Patricia Baird to a conference on neonatal/perinatal medicine, 46 percent of physicians support court-ordered interventions "to enforce the mother's cooperation in treatment of the fetus." See "The Implications of New Reproductive Technologies for the Care of the Perinatal Patient," paper delivered to a meeting of the American Academy of Pediatrics, 24 May 1991, Whistler, B.C.
- 4. When technology is equated with science and blamed for the ills of human civilization, the critics are often dismissed by the powers that be as lunatic and are effectively prohibited from contributing to the re-evaluation and rethinking process. But ignoring the critics in this case can be dangerous, as the anti-science sentiment may well be more deeply rooted than one thinks and can make for a volatile situation of the sort witnessed in the 1930s. German novelist Hermann Broch, commenting on the cultural psyche of that era, wrote, "One of the essential elements of the present era is that it attempts to compensate for the decline in religious faith by an almost feverish worship of nature, on the surface motivated by hygienic, sports related, ecological or other such rationalizations ... One would not be wrong to see in this constant readiness of mythic and nature-oriented tendencies to reassert themselves one of the main reasons why our present epoch is so vulnerable to mass-psychological forces." See H. Broch, The Spell (San Francisco: North Point Press, 1989). Moreover, scientists who view technology as a reflection of social and political culture find themselves in a polarized debate, which makes critical self-assessment difficult.
- 5. U.S., Institute of Medicine and National Research Council, *Medically Assisted Conception: An Agenda for Research* (Washington, DC: National Academy Press, 1989), 15.
- 6. U.S. Congress, Office of Technology Assessment, Infertility: Medical and Social Choices (Washington, DC: U.S. Government Printing Office, 1988), 293.
- 7. In 1988, 17 to 22 million vertebrate animals were used in research, education, and testing in the United States (1 percent of the number killed for food). See U.S.,

Institute of Medicine, Committee on the Use of Animals in Research, Science, Medicine and Animals (Washington, DC: National Academy Press, 1991), 4.

- 8. According to the NAS research agenda, further advances in the field of infertility awaited work on the cell biology and biochemistry of early gamete maturation and fertilization, oocyte maturation, and the biochemistry of sperm capacitation and entry into eggs. Other important research topics include membrane biochemistry, hormonal control of testicular and ovarian function, gene expression in early development, and the cell biology of implantation. See U.S., Institute of Medicine and National Research Council, *Medically Assisted Conception*, 29. See pp. 88-90 for a detailed list of research priorities.
- 9. J.T. Hansen and J.R. Sladek, Jr., "Fetal Research," Science 246 (1989), 777.
- 10. Ibid.
- 11. U.S., Institute of Medicine and National Research Council, *Medically Assisted Conception*.
- 12. Ibid. Despite the leadership role of American research, in this field, as in others, there are differences between the two countries. Fetal tissue can be used for research in Canada, for instance, and the research community is not hampered to the same degree by limitations on the sources of materials for experiments relating to human beings and to animals. In the United States there are also impediments to the *use* of the new technologies: there is only limited health insurance coverage of IVF and embryo transfer services, for instance. In both countries the present dilemma of society in coping with disagreements over ethical standards and principles is an impediment to research.
- 13. Medical Research Council of Canada, Annual Report 1989-90 (Ottawa: MRC, 1990).
- 14. U.S., Institute of Medicine and National Research Council, *Medically Assisted Conception*.
- 15. L. Mastroianni, Jr., P.J. Donaldson, and T.T. Kane, eds., *Developing New Contraceptives: Obstacles and Opportunities* (Washington, DC: National Academy Press, 1990).
- 16. The list is not exhaustive but only illustrative of the types of research activities currently under way. However, it does indicate that only a limited number of researchers are involved in this area of research in Canada, given that the Medical Research Council funds some 2 900 researchers and that, overall, some 8 000 researchers are working in health science research in universities and hospitals across Canada.
- 17. Indeed, many scientists complain that their fields are being starved of support as resources are applied to molecular biology programs. And some science managers are concerned that advances in basic science are occurring so quickly that traditional disciplines such as physiology and biochemistry, on which many of the applications of the new knowledge will depend, are seriously falling behind (private communication, Dr. Machi Dilworth, Program Director for Special Projects, Division of Instrumentation and Resources, National Science Foundation, October 1991).
- 18. Royal Society of Canada, "Prospectus for a Study of Molecular Biology" (Ottawa: The Society, 1993). The committee points out that it is molecular biology that

makes possible genomics, one of the most exciting challenges in the history of science, the study of the biology of organisms through the complete and detailed description of their genetic make-up. Examples of areas where medical science can now explore in its efforts to identify, prevent, and cure disease, based on the use of molecular biology, were recently summarized by Dr. Lou Siminovitch, Director of the Samuel Lunenfeld Research Institute at Mount Sinai Hospital in Toronto. He mentions the roles of proto-oncogenes in the etiology of cancer and cell biochemistry and regulation and development; the roles of protein kinases, photophatases, and growth factors in signalling and other processes; deciphering protein domains in terms of function; identification and analysis of eukaryotic regulatory regions and transcription factors; the beginnings of a molecular pathology based on recent advances in understanding of the lesions in suppression and proto-oncogenes involved in genesis of neoplasia; and the use of transgenic animals and the associated technology of homologous recombination in embryonic stem cells.

- 19. According to Walter Gilbert, Nobel laureate and a former Harvard University professor of biochemistry, genetic sequencing will become a diagnostic tool before the end of the century. "PCR-based small sequencing and the detection of one's own genes will become diagnostic tools much earlier, even in the next five years, and by the end of the century one will be able to sequence 100,000 basepairs, or a megabase, of human DNA and analyze any gene to order for an individual. Soon after that one will be able to go to a drugstore and leave a sample of DNA, and \$300, and get a compact disc that has one's own sequence on it ... I expect that this will happen by the year 2010 or 2020" (W. Gilbert, paper delivered at a meeting of research directors of pharmaceutical companies, Hilton Head, South Carolina, 30 September 1990).
- 20. "Discovery Research Spending Continues to Soar as Drug Industry Outshines Investment Promises," *Research Money* 5 (3 July 1991), 2.
- 21. D. Nelkin and L. Tancredi, "Classify and Control: Genetic Information in the Schools," American Journal of Law and Medicine 17 (1-2) (1991), 51.
- 22. Ibid., 55.
- 23. See U.S., Institute of Medicine, Science and Babies: Private Decisions, Public Dilemmas (Washington, DC: National Academy Press, 1990), 4, for a list of the ethical challenges posed by advances in reproductive technology.
- 24. Fetal tissue has the following properties that make it suitable for research and therapeutic purposes: significant capacity for growth and differentiation, potential for growth in vitro, potential for growth and restoration of function in the host, resistance to oxygen deprivation, which is a significant limiting factor in organ transplantation, ease of transplantation of fetal cells, and an immunological immaturity, which means the transplanted tissue provokes little or no immune response in the host. See M.A. Mullen, "The Use of Human Embryos and Fetal Tissue: A Research Architecture," in Background and Current Practice of Fetal Tissue and Embryo Research in Canada, vol. 15 of the research studies of the Royal Commission on New Reproductive Technologies (Ottawa: Minister of Supply and Services Canada, 1993).
- 25. Private communication, October 1991.
- 26. See B.J. Culliton, "Gene Therapy on the Move," *Nature* 354 (1991): 429, for a discussion of the speed with which gene therapy will become "a potent new force in

medicine." She says that "in just the two years that human gene trials have been underway at NIH, it has become clear that gene therapy is not just for single-gene disorders any more." Many experts have in the past been careful to warn that gene therapy is a long way off and that it is unlikely to be used soon for multi-gene pathologies.

- 27. Today, scientists from all over the world are racing toward the knowledge that will allow society to engineer life: agricultural producers are already exploiting in vitro technologies to enhance the contribution of outstanding producer animals (e.g., dairy cows) by multiplying the number of their progeny, and gene transfer technologies promise "the ability to alter the phenotypic characteristics of food-producing animals"; in Japan, an industrial consortium has been formed to develop environmental products for the next century (e.g., an algae that will be superabsorbent of carbon dioxide); in the United States, the federal Department of Agriculture has poured funds into gene expression centres, which have already become the leading laboratories working on plant molecular biology; and internationally, the race is on to map the human genome, a feat that has been compared to landing astronauts on the moon.
- 28. The government of the United States spends more on research than any other government in the world, more than \$21 billion annually by the end of the 1980s.
- 29. Unpublished draft statement of mission and identification of strategic planning panels and policy parameters. The National Institutes will promulgate their strategic plan in February 1992, according to a private communication with the Associate Director for Science Policy and Legislation, Dr. Jay Moscowitz, October 1991.
- 30. The United States is a barometer in the reproductive sciences, especially because such a small proportion of world expenditures for both training and research in the field is actually made elsewhere (6 percent in 1988).
- 31. Mastroianni et al., Developing New Contraceptives, 6, 79.
- 32. Organisation for Economic Co-Operation and Development, *Science and Technology Indicators*, Report No. 3 (Paris: OECD, 1989). Overall research and development spending grew at a rate of about 5 percent per annum.
- 33. According to J.B. MacAulay, some 45 percent of all scientific papers in Canada are published by health research personnel. Hospitals, including university clinics, account for 13 percent of all scientific papers in Canada. See J.B. MacAulay, "Distribution of Canadian Publication Activity Among Sectors," in *An Indicator of Excellence in Canadian Science*, Statistics Canada Cat. No. 88-501 (Ottawa: Minister of Supply and Services Canada, 1985).
- 34. J.R. Ravetz, Scientific Knowledge and Its Social Problems (New York: Oxford University Press, 1973), 13.
- 35. Ibid.
- 36. U.S. Congress, Office of Technology Assessment, *Federally Funded Research: Decisions for a Decade* (Washington, DC: U.S. Government Printing Office, 1991), 5.
- 37. "In 1958, indirect cost billings comprised 10 to 15 percent of Federal academic R&D funding. By 1988, that share had risen to roughly 25 percent" (U.S. Congress, Federally Funded Research, 24).

38. Scientists, like other individuals, are driven by ambition; they aspire to international recognition and influence within the scientific community. To "make it" within the international community, scientists begin early to strategize how they will make their mark in a promising field of research. This is illustrated by the following passage from J.E. Bishop and M. Waldholz, *Genome: The Story of the Most Astonishing Scientific Adventure of Our Time* (New York: Simon and Schuster, 1990):

Huntington's disease was not a disease where a scientist could make his or her reputation. Other genetic diseases were attracting scientists because they had a foundation of research that offered a good chance of making significant discoveries. Biochemical abnormalities had been found in both cystic fibrosis and muscular dystrophy, showing research potential that an astute young scientist might be able to exploit and thus gain a name for himself.

But, given the dearth of knowledge, any scientist tackling Huntington's disease would have to start from scratch — and there were no clues as to where to start. Moreover, the study of inherited diseases like Huntington's focuses heavily on comparisons of family members who inherit the disease with those who don't. This is time consuming enough in diseases that are apparent at birth; for a genetic disease that strikes in adulthood, it seemed more than anyone could ask. A geneticist tackling Huntington's disease would have to wait two or perhaps three decades to see which of a victim's children inherited the Huntington's gene and which escaped it. In short, a scientist could expect to spend a lifetime studying the disease and its victims without the slightest prospect of making even a small niche for himself in medical history.

39. As noted by Robert Edwards, a prime mover in the development of IVF (see *Life Before Birth: Reflections on the Embryo Debate* (New York: Basic Books, 1989), 169-70):

As for me, it was a practical, scientific outlook that drove me on, convinced we were right to employ our skills as we did. IVF, surrogacy, genetic screening, stem cells, all these offer hope to thousands upon thousands of people. And now, writing out of all this experience in December 1988, how do I see the results of all our work? Has all the effort been worth it? Where do we stand, in the last part of the twentieth century, in relation to scientific advances, the ethical upheavals, the new medical understanding that has emerged from those long years of struggle?

It has certainly been worth it, for some things have been permanently changed for the better. IVF is accepted worldwide for the alleviation of infertility, and will never be outlawed now. Improvements are certainly needed, in particular to help the spermatozoa of men with a low or abnormal sperm count to penetrate egg membrane which in some cases bars fertilisation, but people of every race and religion all over the world have benefitted from IVF.

40. One example of the new structure is Quadra Logic Technologies Inc. of Vancouver, a company that was founded by five University of British Columbia researchers. Another is Genentech; Herbert Boyer of the University of California

was instrumental in the start-up of the company and became a cult-hero in the early 1980s because he suddenly became very wealthy through his research. The line between academic research and commercial development became increasingly blurred. Biologists at the University of California actually mounted a campaign to get Boyer to remove his commercial activities from his department on campus. See E. Yoxen, *The Gene Business: Who Should Control Biotechnology?* (London: Pan Books, 1983), 67.

- 41. Dr. Camille Limoges, Director of CREST at the Université de Québec à Montréal and a former Deputy Minister of Education and Science in the Province of Quebec, notes that since about 1980 so-called science policy has been utterly replaced in government thinking by "innovation policy" (private communication, October 1991).
- 42. The region contains the cities of Lyon and Grenoble and has the highest concentration of high-technology firms (over 2 000) and research organizations in the country, after Paris, of course, where there are nine universities and 240 laboratories. The state of Baden-Wuerttemberg in Germany is another aggressive competitor for outside research funding; this jurisdiction boasts the highest concentration of research institutes in Europe, much of it around the capital of Stuttgart.
- 43. Examples are IBEX Technologies Inc., Allelix Biopharmaceuticals Inc., IAF BioChemInternational Inc., Biomira Inc., and Quadra Logic Technologies Inc. in Canada; and American companies such as Cetus, Genentech, Biogen, Genex, CellTech, and Calgene. In the early days of this industry, it seemed that extraordinary wealth would quickly follow investment in the new technologies. Some people did make a lot of money, but the early optimism of investors waned as the technical difficulties of commercializing genetically engineered medical products became evident. It is now accepted that the pay-offs will be longer term and in specialized niche areas.
- 44. NGL Consulting Ltd.
- 45. Venture capital firms usually invest in the initial two to three years prior to biotechnology firms going to the public market for continued funding. They usually exit with a capital gain when the biotechnology firm goes public.
- 46. "Promises, Promises," The Economist (5-11 October 1991), 69-70.
- 47. Small biotechnology companies typically need one dollar of working capital per dollar of sales. So it is not surprising to see these firms scouring the financial markets and striking whatever deal is needed to ensure their growth. Moreover, the mature pharmaceutical industry operates in a research environment where systematic analysis is undertaken on a large number of possibilities in the hope of obtaining a major winner downstream. As noted elsewhere,
 - from 10 000 preparations, 20 compounds go on to further study;
 - 10 make it to safety and efficacy trials;
 - 5 pass into extensive trials;
 - 2 go on to comparative tests;
 - 1 is retained as worthwhile.
- 48. "Promises, Promises, Promises."
- 49. U.S. Congress, Infertility: Medical and Social Choices.

- 50. See the National Consortium of Scientific and Educational Societies, *Meeting the Challenges of the 21st Century (Appendix 1)* (Ottawa: National Consortium, 1991), for a description of gross expenditures on research and development by all sectors in Canada, 1963-1990.
- 51. Science Council of Canada, *Genetics in Canadian Health Care* (Ottawa: Science Council of Canada, 1991), 94.
- 52. Medical Research Council of Canada, Annual Report, 1989-90.
- 53. Royal Society of Canada, Committee on University Research, Realizing the Potential: A Strategy for University Research in Canada (Ottawa: The Society, 1991), 6.
- 54. E. Ryten, "The Funding of Research Conducted by Canadian Faculties of Medicine," ACMC Forum 24(3) (1991), 1.
- 55. According to the Patented Medicine Prices Review Board, expenditures on research and development by 63 Canadian patent-holding drug companies in 1990 were \$281.3 million, 8.8 percent of the Canadian sales of these companies. See Third Annual Report for the Year Ended December 31, 1990 (Ottawa: The Board, 1991), 19.
- 56. For example, Merck Frosst is in the process of hiring some 200 scientists for its new \$70 million research centre in Kirkland near Montreal, where the company plans to invest \$239 million over the next four years.
- 57. Pharmaceutical Manufacturers Association, New Drug Approvals in 1990 (Washington, DC: PMA, 1991).
- 58. The Canadian biotechnology sector is strong scientifically but lacks the ability to undertake complex clinical trials and to market and distribute its products. There is an attraction for these firms to enter into strategic alliances with the larger pharmaceutical firms that can provide these requirements. A web of relationships is emerging for example:
 - Quadra Logic Technologies Inc. of Vancouver with American Cyanamid (U.S.) and Basic Healthcare Corp. (U.S.);
 - IAF BioChemInternational of Laval, P.Q., with Glaxo (U.K.); and Allelix Biopharmaceuticals Inc. of Mississauga, Ontario, and Glaxo (U.K.) and Eli Lilly (U.S.).
- 59. J. Weldon and D.B. Shindler, Canadian Biotechnology Industry Sourcebook (Ottawa: Ministry of State for Science and Technology, 1988).
- 60. Canada, Industry, Science and Technology Canada, Health Care Products Directorate, *Meeting the Challenge: Implementing the Medical Devices Sector Initiative Phase III* (Ottawa: The Department, 1991). There are a few large multinational firms and many small and medium-sized firms in the sector. Canadian ownership is about 89 percent. These firms are mainly small (sales of less than \$5 million annually and employment less than 50). This industry, like the pharmaceutical and biotechnology industries, is situated mainly in Quebec and Ontario. Canadian production includes ophthalmic goods (35 percent), medical supplies (27 percent), surgical and medical instruments and appliances (18 percent), dental supplies (11 percent), orthopaedic appliances (9 percent), and some others.
- 61. According to Judy Erola, President of PMAC, Quebec has been a model of coordination of various aspects of provincial policy and regulation in order to

provide a stable and positive environment for industrial development in general and investment of funds arising from Bill C-22 in particular (private meeting, September 1991).

- 62. See Ryten, "Funding of Research," for all data on funding of research at medical faculties.
- 63. Medical Research Council of Canada, *Brief to the Royal Commission on New Reproductive Technologies* (Ottawa: MRC, 1991).
- 64. Alan Fine, Presentation on the Fetal Tissue Transplantation Program of Dalhousie University, 20 June 1991.
- 65. Medical Research Council of Canada, Guidelines for Research on Somatic Cell Gene Therapy in Humans (Ottawa: Minister of Supply and Services Canada, 1990) and Guidelines on Research Involving Human Subjects (Ottawa: Minister of Supply and Services Canada, 1987).
- 66. The Health Protection Branch also regulates the use of medical devices, but its activities in this sector have little or no impact on the development of new reproductive technologies. While firms need to notify the Branch of the introduction of new medical devices, review and approval are needed only for contact lenses designed or represented for prolonged wear, menstrual tampons, and any device designed to be implanted into the tissues or body cavities of a person for 30 days or more.
- 67. PMAC has described the situation as follows:
 - Since it takes about three years from date of patent application to date
 of grant, the basic provision in Canada's amended Patent Act of 20 years
 from date of application is equivalent to 17 years from date of patent
 grant;
 - Bill C-22 provided improved protection for intellectual property but did
 not restore full patent protection. The legislation retains compulsory
 licensing provisions, making protection conditional upon compliance
 with the pricing and R&D investment guidelines of the Patented Medicine
 Prices Review Board;
 - the legislation provides no protection from compulsory licences for export from Canada;
 - assuming compliance with the Pharmaceutical Manufacturing Price Review Board, the protection for innovators is limited to the lesser of the remaining patent life, or seven years before a compulsory licence can be used by a competitor to manufacture for sale in Canada;
 - for products on the market when the legislation was introduced on 27 June 1986, the maximum period of protection from a compulsory licence for a competitor to import for sale in Canada is seven years, if either a compulsory licence or a notice of compliance had already been granted to the competitor;
 - where neither was granted, the period is eight years;
 - only medicines invented and developed in Canada receive the full patent protection of 20 years from date of application enjoyed by other industries in Canada.

- 68. According to the Organisation for Economic Co-operation and Development's *Main Science and Technology Indicators* (Paris: OECD, 1989), by 1987 Japan was spending \$378 (U.S.) per person on research and development; 8.1 persons per 1 000 members of the labour force in Japan were classified as researchers. The United States was spending even more per capita on research and development (\$493) and more than \$120 billion in all, 2.69 percent of its gross domestic product in that year. Canadian expenditures on research and development in 1987 in U.S. dollars were \$241 per capita and \$6.2 billion in all.
- 69. J. Niosi and P. Faucher, "The State and International Trade: Technology and Competitiveness," in *Technology and National Competitiveness: Oligopoly, Technological Innovation and International Competition*, ed. J. Niosi (Montreal and Kingston: McGill-Queen's University Press, 1991), 124 (quoting figures from *UN Yearbook of International Statistics*).
- 70. The OTA has suggested that "Congress could instruct every research agency to develop a baseline of [bibliometric data] ... and direct OSTP (in conjunction with OMB) to devise a plan to increase the reporting and use of agency data in the budget process" (U.S. Congress, Federally Funded Research, 41).
- 71. Even experienced industrial research managers like American John Gilman, who directed the research department of Amoco Corporation and is now senior scientist at Lawrence Berkeley Laboratory, have expressed sharp concern about the inappropriate intrusion of government management culture into basic research.

The "Big Brother knows best" approach is irrational because in reality Big Brother knows nothing. That is, he knows nothing about the most important aspect of the research enterprise, namely, the unknown. He knows nothing about undiscovered territories, unconceived ideas, undetermined facts, inventions yet to be made (J. Gilman, "Research Management Today," *Physics Today* 44 (March 1991), 45).

Perhaps the most striking example of the organizational approach in Canada is the federal Networks of Centres of Excellence program, which assumes that scientific leadership will emerge if teams are created first as opposed to giving proven leaders the resources they need to expand existing teams and develop networks appropriate to already defined project needs.

- 72. John Gilman explains the calculation that industry makes as follows: "Because research spending must be subtracted from pretax earnings, a company's value as a continuing source of revenue passes through a maximum as research spending increases. This determines an optimal spending level, which can be calculated by simply maximizing a quadratic equation... Once the optimum has been reached, further increases become counterproductive because they subtract from current production" (Gilman, "Research Management Today," 44).
- 73. OECD, Science and Technology Indicators. In the 1980s, business financing of R&D in OECD countries grew at a rate 50 percent greater than that of government financing, while overall R&D spending grew at a rate of about 5 percent per year.
- 74. As the competition among academic institutions intensifies, there is a corresponding growth in promotional activity. "Public relations often emphasizes the spectacular promises of research in order to attract corporate funds and it is not clear that this hype is, in the long run, good for either universities or science" (D. Nelkin and R. Nelson, "University-Industry Alliances," Science, Technology and

Human Values 12 (1)(1987), 71-72). Scientists have already lost credibility with government decision makers by making unrealistic claims concerning the economic and other practical benefits of their projects (Camille Limoges, private communication, October 1991).

- 75. There are those who argue that science "requires more credulity than the myths it supplants ... No myths about the origins of life or the nativity of the stars are as staggeringly implausible as the accounts of these events we receive from biologists and astrophysicists (F. Burroughs, Jr., "By a Logic That Eludes Us," *Harper's Magazine* (February 1991), 36-39).
- 76. The recent spate of immensely popular cyborg films illustrates the point. Muscle man Arnold Schwarzenegger's Terminator pictures, which feature machines in men, are stories of humanity's struggle against the tyranny of modern machines. The two Canadian-made Robocop films, which feature men in machines, are stories about the danger of technological conspiracy; to carry a basically bloodthirsty adventure tale, $Robocop\ I$ and II rely on brutally comic depictions of the dehumanizing effects of both technology and the media.
- 77. The image of science out there is an intellectual activity that is antithetical to eros. This is more significant than it might seem at first blush. "Simply put, nature is objectified ... The modes of intercourse are defined so as to insure emotional and physical inviolability ... Concurrent with the division of the world into subject and object is, accordingly, a division of the forms of knowledge into 'objective' and 'subjective'" (W.I. Thompson, *Imaginary Landscape Making Worlds of Myth and Science* (New York: St. Martin's Press, 1989), 191).
- 78. M. Ridley, "The Edge of Ignorance Science," *The Economist* (16 February 1991), 17.
- 79. Angus Reid Group, "The Public's Perspective on Science," *Reid Report* 5 (9)(October 1990), 6.
- 80. E.F. Keller, "Gender and Science," in *Discovering Reality*, ed. S. Harding and M.B. Hintikka (Dordrecht: D. Reidel, 1983), 189.
- 81. Ibid.
- 82. Louis Harris and Associates, *Public Attitudes Toward Science*, *Biotechnology and Genetic Engineering* (New York: 1987), 49.
- 83. Ibid., 2.
- 84. Angus Reid Group, "Public's Perspective," 6. "Moves to enhance the profile of scientific research and development would meet with considerable support from the general public."
- 85. Ibid., 9.
- 86. Angus Reid Group, "The Canadian Public's Views on Health Care Issues," *Reid Report 6* (6)(1991), 1.
- 87. Ibid., 9. Even for basic research, though, "exactly one-half of those surveyed said they believed more money should be spent than is currently the case."
- 88. A recent Sussex University Science Policy Research Unit (SPRU) analysis of OECD expenditures on academic and related research by main field in 1987 concludes that the United States spends significantly more (48.9 percent) of its

research budget on the life sciences than any of the other member countries (average *including* the United States is 36.4 percent).

- 89. Louis Harris and Associates, Public Attitudes, 7.
- 90. E. Singer, "Public Attitudes Toward Genetic Testing," paper based on a telephone survey done by Gallup Organization, 1990, 10.
- 91. P. Slovic, "Perception of Risk," Science (17 April 1987), 282.
- 92. Angus Reid Group, "The Credibility of Selected Information Sources," *Retal Report* 46. Scientists/professors were "the only information source of the six assessed for which a majority (61%) of Canadians believe 'most' of what they say concerning the environment." The proportion of the public that favours increased social control over scientific growth and technological progress increased from 31 percent to 43 percent between 1977 and 1987 (Louis Harris and Associates, *Public Attitudes*, 33). It was 28 percent in 1972. Louis Harris and Associates suggest that "a majority of the public might favour increased control within a decade" (ibid., 40).
- 93. Louis Harris and Associates, Public Attitudes, 4.
- 94. Ibid.
- 95. J. Bronowski, The Ascent of Man (Boston: Little, Brown, 1973).
- 96. Thompson, Imaginary Landscape, 20.
- 97. O. Paz, "The New Analogy: Poetry and Technology," in Convergences: Essays on Art and Literature (Orlando: Harcourt Brace Jovanovich, 1987), 124.
- 98. Ibid., 117.
- 99. S. Brand, The Media Lab: Inventing the Future at MIT (New York: Viking, 1987), 9.
- 100. Franklin, Real World, 24.
- 101. Ibid., 29.
- 102. J.L. Finkelstein, "Biomedicine and Technocratic Power," Hastings Center Report 20 (July-August 1990),16.
- 103. D. Nelkin and L. Tancredi, "The New Diagnostics," National Forum (Fall 1989), 5.
- 104. Ibid.
- 105. Ibid., 6.
- 106. Quoted by R. Hubbard in "Science, Facts, and Feminism," in Feminism and Science, ed. N. Tuana (Bloomington: Indiana University Press, 1989), 129.
- 107. R. Macklin, "Artificial Means of Reproduction and Our Understanding of the Family," *Hastings Center Report* 21 (January-February 1991), 5.
- 108. R.G. Evans and G.L. Stoddart, "Producing Health, Consuming Health Care," CIAR Population Health Working Paper No. 6, (Hamilton: McMaster University, Centre for Health Economics and Policy Analysis, 1990), 8.
- 109. A good example of this in agriculture is the February 1991 recommendations of the White House task force on biotechnology policy. The task force, chaired by Vice President Dan Quayle, proposed that new regulations be put into place to deal with the approval of genetically engineered crops, pesticides, and animals. The new

regulations are supposed to simplify the approvals process. The White House Council on Competitiveness is already pressing the Environmental Protection Agency and the Agriculture Department for the regulations to be ready by the end of the year. See *The New York Times* (19 February 1991) for the story on this report. The Quayle report also recommends the preservation of the Orphan Drug Act, which gives exclusive marketing rights to the first company that wins federal approval for a drug that is used to treat fewer than 200 000 patients annually.

- 110. Evans and Stoddart, "Producing Health," 8.
- 111. D. Nelkin, Science as Intellectual Property (New York: Macmillan, 1984), 16.
- 112. James Friesen and Ford Doolittle, submission regarding Canadian participation in the international human genome program, unpublished paper, 1990.
- 113. D. Baltimore, "Keynote Address to the 1988 Meeting of the American Association for the Advancement of Science" (Cambridge, Mass.: Whitehead Institute for Biomedical Research, 1988), 3.
- 114. S.G. Harding, The Science Question in Feminism (Ithaca: Cornell University Press, 1986), 224.
- 115. Ibid., 45.
- 116. Ibid., 109.
- 117. Biology and Gender Study Group, "The Importance of Feminist Critique for Contemporary Cell Biology," in *Feminism and Science*, ed. N. Tuana (Bloomington: Indiana University Press, 1989), 182. And there follows a military analogy: "It appears that an arbitrary genderization of molecules has been made, where one of the colliding molecules is called the 'attacking' group and the other is the passive recipient of this attack" (ibid.).
- 118. Harding, Science Question in Feminism, 120.
- 119. The quotation is from D. Haraway, "Lieber Kyborg als gottin!" in *Argument-Sonderband* 105, ed. B.P. Lange and A.M. Stuby, 1984, 66-84, as quoted in Biology and Gender Study Group, "Feminist Critique," 1989, 180.
- 120. National Science Foundation, *Proposal Review at NSF: Perceptions of Principal Investigators*, NSF Report 88-4 (Washington, DC: NSF, 1988), 4.
- 121. Ibid., 10.
- 122. Royal Society of Canada, Committee for the Advancement of Women in Scholarship, *Plan for Advancement of Women in Scholarship: Report* (Ottawa: The Society, 1989), 13.
- 123. R. Ginzberg, "Uncovering Gynocentric Science," in *Feminism and Science*, ed. N. Tuana (Bloomington: Indiana University Press, 1989), 71.
- 124. Harding, Science Question in Feminism, 134.
- 125. William Raub, Acting Director of NIH, has noted that the definition of health issues that generated that number was quite narrow. He estimated that using a similarly narrow definition for men's diseases would have generated a figure of 5 percent. See *HHS News* (10 September 1990) for the announcement of the establishment of an Office of Research on Women's Health (ORWH). "The ORWH is charged with assuring that research conducted and supported by NIH

appropriately addresses issues regarding women's health and that there is appropriate participation of women in clinical research, especially in clinical trials."

126. Private communication, Cathy McDermott, Executive Director, Grantmakers in Health, New York City, October 1991. McDermott cited the figure \$10 million as the NIH sponsorship of research on breast cancer and expressed anger about the indifference of successive directors of NIH toward women's health issues.

127. Harding, Science Question in Feminism, 22.

128. See ibid., 57, for a summary of this argument. "Feminism proposes that there are no contemporary humans who escape gendering; contrary to traditional belief, men do not. It argues that masculinity — far from being the ideal for members of our species — is at least as far from the paradigmatically admirable as it has claimed femininity to be. Feminism also asserts that gender is a fundamental category within which meaning and value are assigned to everything in the world, a way of organizing human social relations. If we regarded science as a totally social activity, we could begin to understand the myriad ways in which it, too, is structured by expressions of gender. All that stands between us and that project are inadequate theories of gender, the dogmas of empiricism, and a good deal of political struggle."

129. U.S. Congress, Infertility, 179.

130. Ibid.

131. Edwards, Life Before Birth.

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An Overview of Select Social and Economic Forces Influencing the Development of *In Vitro* Fertilization and Related Assisted Reproductive Techniques

Anne Rochon Ford



Executive Summary

The development of *in vitro* fertilization and related assisted reproductive techniques was affected by the two factors discussed in this paper: the interplay between popular perceptions of infertility and demand for the techniques, and the role of the pharmaceutical industry.

While human infertility is not a new problem, the expectation of solutions is new. This changed perception of infertility as a treatable problem is traced through popular women's magazines and the literature of the self-help movement over the past 20 years. Perception of infertility as a female problem has resulted in less attention being paid to male infertility, while the growth of the women's health movement and increased control over reproduction through the use of contraception have led to the belief that women who are unable to conceive have a right to seek help and to be helped. At the extreme, infertility has been characterized as a disability, and the withholding of treatment, therefore, as discrimination. It is these perceptions, rather than any noticeable increase in infertility, that are responsible for increased demands for infertility services, and improvements in technical expertise are, in part,

The pharmaceutical industry, among the most profitable in the manufacturing sector, has played a major role in the field of assisted reproductive technologies. Pharmaceutical companies influence the prescriptive practices of physicians by means of advertising, sales representatives, and the Compendium of Pharmaceuticals and Specialties (the single most widely consulted source of pharmaceutical information by Canadian physicians), and by sponsoring continuing medical education courses, conferences, and post-graduate training. These companies also attempt to reach consumers directly by assisting nonprofit organizations and producing public education materials. These materials provide examples of how the industry portrays women by using sexist and outdated images. In addition, women lack involvement in decisions about drugs that will affect them, have no real control over how drug research is formulated, carried out, and interpreted, and are present in the industry only at entry-level positions. While there have been improvements in how the industry operates, the potential for abuse and harm is still high, and there is a need for continued observation by critics.

Reproduction is ... unique in that it is the only bodily function not essential for the maintenance of an individual's survival ... Because it is the only bodily function that is different in men and women, it lies at the heart of debates about gender.\(^1\)

Introduction

Among the various tasks mandated to the Royal Commission on New Reproductive Technologies in October of 1989 was that of examining "the implications of new reproductive technologies for women's reproductive health and well-being." While these technologies can and do have a profound effect on men and children, women, as the primary recipients of the techniques and as the bearers of children, shoulder the greatest burden. Women benefit most directly from the techniques when they are successful, but when they fail, it is women who are the victims and who tend to suffer the greatest loss. It is primarily women who lobbied for the creation of this Commission, and it is women who have been its strongest

critics. Women are also the nurses, the technologists, and, sometimes, the physicians who work with these technologies. And it is women who have been the victims of medical and pharmaceutical mistakes in the past — diethylstilbestrol (DES), the Dalkon Shield[®]. When we evaluate the implications of new reproductive technologies for women's reproductive health and well-being, we must extend the net far and wide to consider women in many roles and in a larger social and historical context.

In a study of the social meanings of new technologies and how they come to be accepted by a wider public than the scientific community, American author David Nye states: "Every new technology is a social construction and the terms of its adoption are culturally determined." The term "social construction" is used here to refer to the fact that a web of social, economic, and cultural factors is an integral part of the development or creation of that technology. Similarly, the Office of Technology Assessment report on infertility noted: "infertility is not only a personal medical problem, but also in some ways a social construct." When we consider the implications of the new reproductive technologies for women, we must bear in mind the social factors that influence our perceptions of infertility, of these technologies, and of women.

With this backdrop in mind, this paper examines some of the factors that continue to influence the development of *in vitro* fertilization (IVF) and assisted reproductive techniques (ARTs). Part 1 begins with an analysis of the literature that some women consult in relation to their health. This includes mainstream women's magazines, the literature of the infertility self-help movement, and women's health movement literature. These sources are considered with a view toward better understanding both how public perceptions of infertility have changed over the past 20 years and the effect that this has had on the development of the new reproductive technologies.

Public perceptions about infertility are considered in light of a pervasive notion of an "epidemic of infertility," a notion perpetuated primarily by the media. This notion of an epidemic is challenged, and alternative reasons for the *belief* that there is an epidemic are offered. Consideration is given to the reasons why infertility is largely presumed to be a woman's problem, and why so much less is known about male factor infertility, in spite of its importance.

Infertility and the new reproductive technologies are increasingly being discussed in the context of choice and a woman's right to choose these technologies. The origins of this thinking are examined, as well as the shortcomings of the argument that if women have the right to choose abortion, they should have the right to choose any of the technologies. The growing acceptance of the belief that infertility is a disability, and that those who are infertile should be treated with the same consideration given to other people with disabilities, is also examined.

In Part 2, the influence of the pharmaceutical industry both on women's reproductive health and on the development of the new

reproductive technologies is investigated. This is done through an examination of the operation of the industry in Canada and the means used for marketing its products. The importance of pharmaceutical products related to women's reproduction is examined, as well as the legacies — both harmful and helpful — left by those products.

Reference in the text to "new reproductive technologies," unless used in a broad and general sense, is intended to mean IVF and related ARTs (i.e., technologies intended for infertile individuals and not those related to

prenatal diagnosis and embryo and fetal tissue research).

Part 1. The Changing View of Infertility in the Context of Assisted Human Reproduction

Human infertility is not a new phenomenon. Since the beginning of recorded history, accounts of infertility have been documented. What is new is that for the first time we see infertility defined as a medical condition that is potentially treatable through medical means. The generation of Canadians born during the post-war "baby boom" years is now the first generation of adults able to find some solutions to fertility problems. This is also the first generation to *expect* solutions to their fertility problems.

Advances made in reproductive technology over the past 25 years have occurred at a phenomenal pace, and social analysts and ethicists have been hard pressed to keep up with the critical analysis needed in this field. For many Canadians, these advances in reproductive technology are seen as positive developments that are nothing short of miraculous. The rapid development of the technologies has been viewed by many as a logical response to what some have called an "epidemic of infertility." On the other hand, feminists and other critics of the status quo have challenged those perceptions on a number of fronts, and their questioning has had a distinct impact on the public view of these technologies. 6

For example, the notion of an epidemic of infertility has been challenged by many experts and writers in this field. An acknowledged shortcoming of a number of studies of fertility and demographic change in Canada and the United States over the past 25 years has been the absence of information on actual rates of infertility. Whatever rise there may appear to be in infertility may be caused by the fact that more women are postponing childbearing until after 35, when fertility naturally decreases. It is hoped that the work of the Commission will clarify the extent of the

supposed "epidemic" in Canada.

Whether infertility is truly on the rise in Canada or whether the changes we see are solely demographic shifts, public perceptions of infertility have changed measurably over the past 25 years. This paper examines the particulars of that change in perception, discusses some of the markers of the changes, and proposes some explanations for those

changes. It is anticipated that such an examination will be useful to the Commission in illuminating the current context in which many deputations to the Commission were made. This examination involves looking at popular women's magazines in the French- and English-Canadian press, and the literature of the women's health movement and the infertility support movement, as well as providing a synthesis of contemporary writings on this topic. It is hoped that this information will be useful to the Commission in its deliberations over recommendations related to social policy concerning infertility and the new reproductive technologies.

The topics covered in Part 1 overlap the mandates of Working Group 1 (Causes and Prevention of Infertility) and Working Group 2 (Methods of Assisted Human Reproduction) of the Royal Commission on New Reproductive Technologies. It is intended, in part, to provide a bridge between these two groups.

Part 1 contains elements of empirical research and provides a summary of key issues drawn from existing literature relating to changing views of infertility in light of the new reproductive technologies. This section begins with the empirical research.

Changing Views of Infertility in Canadian Women's Magazines

With circulation figures in the hundreds of thousands, the category of magazines referred to as "mass circulation women's magazines" represents a significant force in influencing the opinions of Canadian women on a wide range of topics. These magazines are an important measure of the knowledge of literate Canadian women about issues related to their health and well-being. A 20-year look at the coverage of infertility and the new reproductive technologies sheds some light on what Canadian women have been reading and thinking about these issues. Mass circulation magazines do their best to provide readers with topics market research has determined to be popular. According to one study, Canadian women do rely on popular women's magazines as a source of information in making decisions about their health care, ¹⁰ in particular regular columns on health issues and feature articles.

To this end, three Canadian magazines — two from the English press and one from the French press — were examined to determine the extent of their coverage of infertility-related issues over a 20-year period. Articles were not read in their entirety; rather, titles were documented and articles were read only if necessary to determine if the title reflected the content of the article. The magazines were selected on the basis of readership figures, these three being among the most popular women's magazines in Canada. (See readership data below.) Using 1978 as a watershed year — the first year a woman gave birth to a baby, Louise Brown, conceived through IVF — coverage of infertility-related topics for the 10 years preceding and 10 years following was explored. Notation was made of any columns or feature articles relating to infertility as listed in the tables of contents. Key

words for the search included infertility, motherhood, maternity, pregnancy, wanting babies, contraception, new reproductive technologies, in vitro fertilization, test tube babies, Louise Brown, surrogate mothers, and artificial insemination.

Findings

The tables of contents for all issues of Chatelaine magazine 900 000; total readership: 2 703 000), Homemaker's¹¹ (controlled circulation [i.e., free distribution]: 1 600 000; subscribers: 8 000), and Châtelaine (circulation: 200 000) were examined for the period of 1968 to 1988.12

Readership of all three magazines is predominantly female. 13 Chatelaine, with the highest female readership of any Canadian magazine, is read by approximately 2 117 000 women (78 percent of the total readership) and 586 000 men (22 percent). Châtelaine has an average readership of 803 000 per issue, 71 percent being women and 30 percent being men. Homemaker's is read by an average of 1 576 000 people,

81 percent being women and 19 percent being men.

In terms of the actual number of articles on infertility and related topics, there was a notable increase from the late 1960s to the 1980s in all three magazines. The first article on infertility appeared in 1969 (Chatelaine), with minimal coverage throughout the 1970s, increasing in The first articles about any forms of assisted human reproductive techniques were about artificial insemination in 1971 (Châtelaine) and 1972 (Chatelaine), followed by coverage of the birth of Louise Brown in 1978 in the two English-language magazines. The number of articles about ARTs increased in all three magazines after 1978. The first article on surrogacy appeared in 1980 (Homemaker's).

The first column on an issue related to male fertility appeared in 1979 (Homemaker's), and the only other article devoted to the subject appeared in 1985 (Chatelaine). Articles and columns that addressed harms to fertility - sexually transmitted diseases (STDs), pelvic inflammatory disease (PID), and occupational reproductive health hazards — appeared with more frequency in the three magazines in the 1980s. Coverage of the issue of adoption also increased in the 1980s in Chatelaine and Châtelaine.

Articles relating to "delayed childbearing" appeared consistently throughout the 20-year period in Chatelaine ("How the Biological Clock Runs Your Life," December 1968: "20s, 30s, 40s ... What's the Ideal Age to Have a Baby?" November 1982), while the French-language Châtelaine focussed more on contraception and limiting family size ("Bye bye grosses familles," April 1975). A noteworthy distinction between the English- and French-language magazines was a tendency in the French-language magazines to carry more articles on questions of the medicalization of childbirth and unnecessary or questionable gynaecological surgeries ("Utérus: On coupe, Madame?" February 1984). 14

Discussion

An examination of titles of articles in popular women's magazines is limited in its ability to provide an in-depth look at the issues in question. The examination of only Canadian magazines also has its limitations since we know that Canadian women read a great many American women's magazines, notably *Woman's Day, Redbook*, and *Good Housekeeping*.

Such an examination does, nonetheless, provide a sketch of the issues covered and of the frequency of coverage. The tone of article titles conveys a range of opinions toward new reproductive technologies, including messages of support ("Née en douceur dans un amour d'hôpital," Châtelaine, May 1978), concern ("Frozen Sperm: Risk of Abnormal Babies?" Chatelaine, October 1972), disapproval ("Our Shocking Failure in Birth Control," Chatelaine, November 1972), victory ("A Baby At Last!" Chatelaine, April 1985), and defeat ("When the Stork Doesn't Arrive," Homemaker's, November 1981).

This examination of three Canadian mass circulation women's magazines adds some information to the analysis of the factors that have contributed to Canadian public opinion in relation to infertility and the new reproductive technologies.

The following is a distillation of the findings from this review of the magazines. (Since the readership is predominantly female, we might assume that the impact has been primarily on women. Nonetheless, a significant number of men also read these magazines [see figures above], and even men who do not may be influenced by their partners' reading of them.)

- 1. Canadian women are concerned about their reproductive health.
- 2. Canadian women are concerned about when to have children and how many to have.
- 3. Canadian women have been exposed to an increasing range of information related not only to the practical details of infertility and the new reproductive technologies but to the social and ethical questions that these issues raise.
- 4. Canadian women are exposed to a great deal of information about developments in treatments for infertility, as well as about medical developments related to other areas of obstetrics and gynaecology, through their monthly reading of mass circulation women's magazines such as these.

This examination of the coverage of issues related to infertility by three Canadian magazines was intended to show a way in which some Canadian women may be receiving information about this issue. Magazines are only one means by which women gather information about issues in which they are interested, and non-written forms of information would provide an equally important area of investigation.

We have observed that coverage of these issues has increased over the 20-year period examined. However, we do not know with certainty whether the coverage increased *in response* to readers' growing interest in and knowledge of the issues, or whether the coverage itself *contributed* to readers' interest in and knowledge of the issues. (These are not mutually exclusive; a combination of both possibilities may be the case.)

A further examination of these articles could involve a deconstruction of the coverage and content of articles, as well as the language, voices, and personalities represented in these articles. Additionally, an examination of the coverage of infertility and new reproductive technologies in the British popular press (publications such as *Women's Weekly*, which enjoys a notable readership in Canada) may provide some insights into Canadian women's knowledge of these issues.

Through the Lens of Personal Experience: Literature of the Infertility Support Movement

This section will examine two publications of the infertility support movement: *Infertility: A Guide for the Childless Couple*, and the newsletters of the Infertility Awareness Association of Canada (IAAC).

Although they are not abundant in Canada, self-help and support groups for individuals experiencing infertility have a place in the Canadian health care system. They range from small groups of four to eight people who meet purely on an ad hoc basis for mutual support, to national organizations aimed at providing both support and information through an extensive network and regular newsletters. These groups are part of the larger movement of self-help and support groups that grew out of the consumer health movement of the 1970s. Not only do they provide an invaluable service to infertile women and men, they have also helped to make the general public more aware of the pain of infertility.

Many groups point to the largest American support group for infertile individuals, RESOLVE Inc., as both the originator of the movement and the model to follow. The founder of RESOLVE Inc., Barbara Eck Menning, is also the author of one of the most popular books on infertility, *Infertility:* A Guide for the Childless Couple. First published in 1977 and then again in 1988, the book not only is a reliable source of information for many infertile individuals, but is frequently cited in writings on the subject of infertility.

The only infertility support group in Canada that claims to be national in scope is the IAAC, in Ottawa. ¹⁵ In existence since 1985, originally under the name of the Infertility Self-Help Support Group (ISSG) and operating out of the offices of Planned Parenthood Ottawa until 1990, the group has regularly produced a newsletter for its members. The IAAC receives partial funding for the production of its newsletters from Serono Canada, distributors of a number of key drugs used in infertility treatments. (See Part 2 for more on Serono.) Basing itself on its American counterpart,

RESOLVE Inc., the IAAC has recently received federal funding allowing it to undertake national outreach. The collected newsletters, containing scores of personal testimonies, provide an important source of information about the experience of infertile couples and reveal interesting insights into public perceptions about the new reproductive technologies.

A closer look at these two sources — the first and second editions of Barbara Eck Menning's Infertility: A Guide for the Childless Couple, and six and one-half years of issues of the ISSG/IAAC newsletters - reveals a primarily enthusiastic, though cautious, approach to the developments in reproductive technology that have occurred in the past decade. Menning notes in the preface of her second edition that so many medical changes had occurred between the two editions that it became necessary both to completely revise the medical sections of the book and to add an entire chapter entitled "New Technologies." This new chapter contrasts sharply with the first edition, published at a time when "there was little between medical articles featuring white-rat research and molecular language and the opposite extreme of sensational and poorly researched stories in popular magazines."16 Although Menning attempts to present information about the new technologies in an unbiased fashion, the foreword to the second edition, written by Dr. Isaac Schiff, Director of the Infertility, Endocrine, and Menopause Unit at the Brigham and Women's Hospital in Boston, is much more enthusiastic in its tone. Schiff notes that "surely there is more reason for celebration than there is cause for alarm with current advances in the field."17 Menning is not quite so optimistic:

In the case of the normal infertile couple, there is nothing conclusive. Years can be spent in a wasteland of suspended animation. There is no pregnancy. There is no known loss, so they cannot grieve and move on. They may shop from doctor to doctor, even country to country, in search of their answer.¹⁸

Of IVF specifically, a technique that was only on the horizon when her first edition went to press, Menning notes in a somewhat cautious tone in her second edition: "There has been no more controversial method of applying technology to infertility than in vitro fertilization."

Schiff's foreword to the book also demonstrates a trend in health care that came to prominence in the 1980s and that has had considerable impact on the way many individuals approach their experience of infertility — the movement toward a belief that consumers of health care have a *right* to treatment for their infertility:

RESOLVE groups are not formed just to encourage anger and catharsis, but to hold each individual and couple responsible for asking for what they need and for trying to achieve it ... The days of "doctor as God" are over. Doctor as "partner in care" has come of age. We ought to be very grateful. 20

As we will see later, and as was demonstrated in some deputations to the Commission, the notion of a *right* to treatment involving costly techniques is controversial. Nonetheless, it may well be a significant contributor to the current demand for treatment.

Infertility support groups such as RESOLVE Inc. and the IAAC have always been grounded in the belief that couples should be presented with as much accurate information as possible and supported in whatever choices they decide are best for them. With each passing year, however, the decisions have become more and more complex. These decisions concern not only whether to embark on any medical treatments at all, but also when to stop or where to draw the line. An entire issue of the IAAC newsletter in 1990 was devoted to the theme "When is Enough, Enough?" As the technologies have become more widespread and as the debate about use of the technologies has become more intense (particularly with the establishment of the Commission in Canada), organizations such as the IAAC have been forced to become more specific in either their support or their condemnation of the new reproductive technologies, as witnessed by the organization's presentation to the Commission in September 1990:

IAAC neither advocates for or against any NRTs or other options available to infertile individuals. IAAC supports individuals and couples in the legal choices they must make in order to establish a family or discontinue treatment ... IAAC supports those individuals and couples who wish to exercise the choices available to them through NRTs to build families ... For those individuals who have been denied the biological facility of family planning, the glimmer of hope rests in the technologies available. These technologies are not without recognized risk, both physical and emotional, and therefore IAAC recommends that this Royal Commission support and promote the safe and responsible use of NRTs. ²²

The pages of the newsletter of the IAAC reveal an organization that wants to provide a forum for all opinions on infertility and access to new reproductive technologies. Past articles include the full range of viewpoints, from major indignation about the harms caused by the technologies to unqualified support of them. Headlines calling out "Bring the IVF/GIFT Clinic to Ottawa!" (Volume 3, Number 6, 1987) are counterpointed by ones such as "Test-Tube Baby-Making Technology Arouses Fears" (Volume 4, Number 4, 1988). With the announcement of the Royal Commission on New Reproductive Technologies, the May-June 1989 issue admonished its readers to "act now ... [since] we stand a fair chance of losing the technologies that we now have access to." One issue contained four pages on pharmaceutical treatments excerpted from a pamphlet produced by Serono Laboratories, in whose interests it is to present the information in the most positive light possible (Volume 1, Number 2, 1985).

Publications such as *Infertility: A Guide for the Childless Couple* and the newsletters of the IAAC provide a much-needed source of information for women and couples experiencing infertility and trying to better understand their experience. A review of all back issues of the IAAC newsletter uncovers a world of tremendous pain and despair. As a support

mechanism, the newsletter attempts to provide its readers not only with tools for coping but also with signs of hope, usually in the form of medically assisted reproductive techniques. Overall, the newsletter appears to present a more positive than neutral or critical view of the technologies. The extent to which this orientation might be influenced by the organization's partial funding by Serono would require more lengthy investigation.

Our Bodies, Ourselves²³

The women's health movement in Canada has its roots in the late 1960s and early 1970s, primarily in the form of small groups of women getting together "to talk about birth control and sexuality and organizing to provide such services as abortion information and referral." Canadian resources produced in the early days of the movement included the Montreal Health Press Inc.'s Birth Control Handbook (1968) and the Women's Health Booklet (1972), produced by a group of women who went on to form the Vancouver Women's Health Collective. During this same period, the Boston Women's Health Book Collective in the United States printed the first edition of the popular handbook Our Bodies, Ourselves (1971). As will be argued later, publications such as Birth Control Handbook and Our Bodies, Ourselves, coupled with the activities of similar women's health organizations, have had a marked impact on Canadian women's health care knowledge and on how women's health issues are covered in the popular press.

Now in its third edition²⁵ (1984), *Our Bodies*, *Ourselves* provides a noteworthy barometer of changes that have occurred in the perceptions of infertility and the new reproductive technologies. For the purposes of this paper, the author compared the coverage of infertility and the new reproductive technologies in all three editions of *Our Bodies*, *Ourselves*.

Nearly half of the first edition (1971) was devoted to pregnancy, childbirth, and the post-partum period, while the subject of infertility warranted a mere two and a half pages at the end of this section. The perception of infertility is reflective of the times in which this edition was published. The authors give credence to the possibility of "psychogenic infertility," noting: "This means simply that because of conscious or unconscious anxieties or fears, a woman will try all kinds of ways not to have a baby"²⁶ and that "it might be that just going to see a doctor will relax you enough to conceive."²⁷

Unruh and McGrath point out that hypotheses of "psychogenic infertility" were particularly prevalent from 1940 to 1970, although by the 1960s, they note, "it was apparent that many of the studies, which had been used to support these hypotheses, did not stand up to methodological

scrutiny."28 They add that

There is no research evidence to support any contentions that stress, other than truly extraordinary stress, causes infertility, nor has infertility been rectified by holidays, adoption, relaxation, or psychotherapy.²⁹

The belief that a positive mental attitude is all that is needed to overcome infertility is one that persists today. Williams noted in her study of women going through IVF that they were repeatedly told by medical staff and other IVF patients that if they did not "think positive," it would not work.³⁰

The relationship between psychological and physical conditions is only a budding area of research in most disciplines of medicine. More research is needed with respect to what influence, if any, psychological factors might

have on infertility.

The second edition of *Our Bodies*, *Ourselves* (1976) contains only slightly more coverage of the issue of infertility, included in a chapter entitled "Some Exceptions to the Normal Childbearing Experience." Note is made of male infertility as a problem not to be ignored, in an attempt to counter the myth that infertility is only a woman's problem. The notion of psychogenic infertility, emphasized in the earlier edition, is played down in this edition, in that stress is given as only one factor among many that may affect fertility. The authors go even further to undo what was written in the first edition: "You might be told your problems are all in your heads. This kind of attitude is not helpful at all." Instead, they attribute unexplained infertility to as-yet-undiscovered physical problems.

As with the first edition, no mention is made of IVF, this still being before the birth of Louise Brown. Artificial insemination by partner and donor is discussed briefly; it is referred to as a difficult choice with "important legal, moral, religious and philosophic aspects to consider." The chapter concludes by reminding readers of the need for infertile couples to press for more research on infertility. A noteworthy addition in the 1976 edition is the suggestion that "you have the right to consider yourself infertile whenever you begin to feel concerned that you are not pregnant." This advice may be problematic, since many women begin to worry if they do not conceive within the first few months of abandoning birth control. The suggestion is made of IVF, this still being being being a difficult choice with the first few months of abandoning birth control.

This suggestion that infertility can be self-diagnosed whenever a woman is concerned about it is repeated in the third edition of *Our Bodies*, *Ourselves* (1984). In contrast with previous editions, this one contains a full chapter on new reproductive technologies and seven pages on infertility. While some forms of infertility are referred to as "curable" in the first edition, they are called "treatable" in the third edition, possibly reflecting a better understanding of just what the new reproductive technologies can and cannot do. (As Williams has pointed out, IVF does not actually treat infertility; it bypasses it. "Even if a woman should be lucky enough to bear a child through IVF, she still remains infertile, since the condition that made her infertile in the first place has not been 'cured.' "35) A number of topics related to infertility and the new reproductive technologies are expanded upon in this edition, including a longer discussion of emotional responses to infertility, which are, in part, reflective of the social pressures on women to conceive, regardless of desire or circumstance.

Discussions of IVF in the third edition contain considerable detail, which reflects the growth in knowledge of the technique during a relatively short time. Detailed descriptions of this and other forms of medical treatment both provide frank information about known side-effects and raise concerns about unknown long-term effects.

Various editions of *Our Bodies*, *Ourselves* can be found on the bookshelves of thousands of Canadian women and in public libraries. Although the book's full impact on women's decision making has never been measured, the book is, nonetheless, a resource that many women have consulted over the past 20 years. For this reason, the book's perspective on infertility and the new reproductive technologies is worth noting, as it has likely enhanced Canadian women's understanding of these issues. The perspective and presentation of infertility and the new reproductive technologies in *Our Bodies*, *Ourselves* can be summarized as follows:

- 1. Infertility is a life crisis for many women. The pain of infertility is real and must be believed.
- 2. The general understanding of the causes of infertility has increased in recent years.
- 3. It is important to reach out to others for support during a crisis such as infertility.
- 4. Infertility can stem from problems within men's bodies as well as women's.
- 5. For many, infertility is a treatable condition.
- 6. Women have the right to shop around for competent and compassionate medical care or treatment for infertility.
- 7. Women have a right to stop treatment at any point along the way. To help in this decision, women are encouraged to periodically reevaluate the importance to them of bearing a child.
- 8. Women have the right (and are justified if they so choose) not to accept treatment for infertility, and to consider adoption or childlessness instead.
- 9. How women respond to their infertility is strongly influenced by society's pressure on couples to have children.
- 10. New reproductive technologies have the potential to help some women to have their own biological children. It is a woman's right to access these technologies, but women are also justified if they choose not to.
- 11. Techniques such as IVF are experimental in nature and carry inherent risks.

12. High-technology solutions to the problems of infertility are problematic. Emphasis should be on prevention.³⁶

The changing view of infertility and the means of treating it as reflected in *Our Bodies*, *Ourselves* is representative of a trend in the women's health movement over the past 20 years, as described by Mellow in 1989:

Over time, the women's health movement has seen a change in ethics from a near absolute rejection of technology, in line with the common meaning of Luddite,³⁷ to an ethic of knowledgeable choices about appropriate technology much more akin to the real legacy of the Luddite movement, [i.e.,] the Luddites' focus was not antitechnology, but against the negative impact of the use of such technology.³⁸

There are some noteworthy distinctions between how some issues are presented in *Our Bodies*, *Ourselves* and the newsletters of the IAAC. Details of the problems experienced by women taking the drug clomiphene citrate, for example, contrast sharply with the description provided by Serono Laboratories in one issue of the IAAC newsletter. The IAAC newsletter maintains that "the occurrence of 'hot flashes' is not a side effect, but rather an indication that the drug is working." In a discussion of IVF, the authors of *Our Bodies*, *Ourselves* acknowledge that IVF has helped or has the potential to help certain women who want their own biological children, while also offering a critical perspective in terms of women's lack of control over the process, the inaccessibility, the physical and psychological invasiveness, and the additional guilt and pressure that the presence of the procedure places on infertile women. As noted above, the IAAC newsletters tend to offer a much more wholehearted acceptance of the procedure.

Perceptions of Infertility in Light of the New Reproductive Technologies

To understand how the introduction of new reproductive technologies has affected societal perceptions of infertility, it is important to place women's experience of infertility in context. Although it is now well documented that the fertility problem of many couples lies with the man, women appear to bear the greater share of the burden of infertility for the couple. For example, one study of IVF in London, England, in 1986 looked at 118 couples being treated for infertility caused by a mix of male and female factors. The study found that women who responded to the questionnaire were significantly more anxious, had lower self-esteem, and were less hopeful than their male partners. In counselling groups, the women described themselves as being "on trial" and saw the infertility as their own problem. 41 Similarly, a member of the Vancouver Infertility Peer Support Group noted in testimony to the Royal Commission on New Reproductive Technologies in November 1990: "We find within our group that when male fertility issues are discussed it is usually the wife [who] will speak on Itheir behalfl."42

In an ongoing study at the University of Michigan examining life quality, psychosocial factors, and infertility, Andrews et al. found that, among the men, "the impact of fertility problems is not fundamentally different from the impact of other problems" in their lives. However, the women perceived a considerable difference between a fertility problem and other life problems. The authors noted that "fertility problems are interpreted as carrying a special negative message for wives' sense of self-and sexual-efficacy."⁴³

While there is substantial documentation of the greater impact of infertility on women than on men, there is no doubt that men also experience distress related to infertility. A study carried out at the Hôpital St-Luc in Montreal found, firstly, that "infertile women showed higher distress than their partners on a global measure of psychiatric symptoms and subscales of anxiety, depression, hostility, and cognitive disturbances, as well as on measures of stress and self-esteem."44 However, although, using a number of measures, women were found to be more distressed than men, men's levels of distress were not insignificant. When the data on both men and women were compared with a larger body of data on the health of Québécois(es) — Santé Québec — it was noted that women report significantly more distress than do men in the general population; however, the men studied in the infertility group displayed more distress than did men in the general population. Hence, while women appear to experience more distress than do men in relation to infertility, both men and women with fertility problems experience more distress than do their peers in the general population.

This latter study also offers some explanations for the differences between the male and female experiences of infertility. These are

summarized as follows:

1. The responsibility for conception and delivery of babies rests "much more on the shoulders of women than men and ... women feel more responsible for the etiology of infertility, even when the medical causes are male."

- 2. Modern medical treatments are more intrusive for the female (time-consuming, painful, risky) "even when the etiology is male-linked."
- 3. Men and women have different ways of dealing with stress; women tend to ruminate more and talk about the distress, while men will try "to forget (deny) the problem by remaining active." 45

Additional reasons for the differences between male and female experiences of infertility have been offered by other authors. As *Our Bodies*, *Ourselves*, the newsletter of the IAAC, and the pages of the popular women's magazines examined here demonstrate, the experience of infertility is one that has been given far more attention by the women experiencing it than by the men. While this has been mostly to the benefit of women

(making them more informed, and allowing them somewhat more control over their bodies), it has also worked, in one way, to women's detriment. By placing so much emphasis on what happens to women through this experience, the fact of male infertility and how men experience it has been minimized. Pfeffer argues that the women's health movement, for all its important gains made for women, has also lost something in its efforts to expose medical control over female reproductive physiology. By placing so much emphasis on this point, she argues, male reproductive physiology has been erroneously seen as structurally efficient with functions that proceed smoothly. She asserts that while "medicine highlights the potential for reproductive disorders in women, it makes them invisible in men." By this, Pfeffer means that perhaps undue attention has been placed on exploring what can go wrong with the female reproductive system in relation to infertility, while problems related to the male reproductive system are overlooked or understated.

Just as the focus of contraceptive technology has been on women, so has that of assisted reproductive technology. As bearers of children, women's reproductive role has always been more obvious than that of men. Although male reproductive problems account for a significant proportion of all infertility problems, women tend to be seen as the source of the problem. As the research of Collins et al. has shown, couples in Canadian infertility clinics were more likely to abandon treatment measures when the source of infertility was with the man. This research also acknowledges that standard treatment is insufficient to overcome male infertility.

We have seen that men's and women's experiences of infertility can differ markedly, in part due to their generally differing responses to stressful life events and their socialization in relation to parenthood. Men's and women's physical experiences of infertility are also quite different, with therapies for women currently being far more invasive, and with far less being known or researched in relation to male infertility.

Infertility and the Question of Women's Control over Reproduction

Why does the experience of infertility appear to be both different and more difficult for women? The simplest answer to that question is that reproduction and motherhood are seen historically to be "central to women's identity and self-esteem." Although women have made considerable strides toward carving out new roles for themselves, the imperative of motherhood holds on tenaciously. One infertile woman on an in IVF waiting list described the pressure this way:

She felt haunted by family and friends who made her feel guilty that she wasn't doing enough to have a baby. "It was almost a relief to be on the waiting list," she says, "because then I could tell all of them that we were doing everything possible to have a child." 52

Feminist thinkers have long embraced the notion that the motherhood imperative has been oppressive for women. Much of the collective energy of the women's health movement over the past 25 years has been

concentrated in helping women to have more control over their reproduction, specifically by *preventing* pregnancy. These advances have been hard-won and have had a profound impact on liberating women from unwanted pregnancy and enabling them to pursue other goals in their lives. The revised report of the UN Decade of Women, released in 1985, notes that "the ability of women to control their own fertility [is] an important basis for the enjoyment of other rights." Although perhaps not evident to many, the women's movement has directly or indirectly affected the lives of most women in Canada. It has done this by lobbying for better access to abortion and to safer and more effective contraception, through its influence in insisting that women should have more control over their childbirth experiences, by lobbying against dangerous reproductive drugs and devices, and through an acknowledgment of women's true experiences of premenstrual syndrome (PMS) and menopause.

Women and men who have come to sexual maturity since the 1960s have been the first generation in history to have a considerable degree of control over their decisions as to whether and when to have children. This sense of control over reproduction⁵⁴ has enabled women, in particular, to feel a sense of control over their lives and has given them a new ability to plan other areas of their lives. Menning begins her book on infertility by noting that "people have never been more in control of their lives" and that some people now plan their families "as meticulously as they do their financial investments, a move to a new location, or a career change — measuring all the pros and cons and waiting until all the elements are just exactly right." ⁵⁵

Thus, for many women who put aside birth control with the decision to become pregnant, the experience of infertility comes as a harsh slap in the face. One writer describes the experience in this semi-fictional account:

Then she "determined" she had had enough of that, now she was going to have those babies, now she was ready, mature, self-realized. And then, Bang. Her world shattered. Her decisions meant nothing, her philosophy went on strike, her body rebelled. Against her.⁵⁶

Others have documented the same sense of betrayal of their bodies: "I was determined to conceive the first month, but quickly learned that determination doesn't work as well with conception as it does in other situations." ⁵⁷

Not only have today's infertile women grown up with the belief that they can control their reproduction, they also believe that they have a right to seek help and to be helped. The women's health and the larger consumer health movements have admonished women and men to exercise their right to get a second opinion. In Canada, the present generation is the first to come of age with a health care system based on the belief that health care is a basic right and, therefore, should be universally accessible. In addition to that belief, a strong consumerist ethic in North American society has led many to believe that we should always get what we want, when we want it.

As medicine moves increasingly into the field of treating fertility problems, ⁵⁹ women and men have come to see medical professionals as the people to turn to for help. Raised in an era in which many medical mistakes involving women's and children's health came into public view, ⁶⁰ many women have been taught to ask questions, to read literature about their condition, to talk to others about it, and to determine a doctor's credentials in dealing with their case. ⁶¹ As Ottawa fertility specialist Arthur Leader notes: "Twenty years ago, these people wouldn't approach a physician. The feeling was that if you couldn't get pregnant, it was God's will." But today, he says, the typical couple is unwilling to give up so easily. "They are couples with established careers who have paid off their mortgages and have now decided it's time to have children. They're 32 and want to have their children before 38, and they want two children — a year or two apart — and they want to know what I'm going to do about it."

In Leader's description of the infertile couple, he builds a case for the argument that medical professionals working in the area of assisted human reproduction are simply giving women and men what they are demanding. Others, however, have argued that the reasons why the medical profession is moving so quickly into the field of assisted human reproduction, and the reason why infertility has come to be seen as a greater crisis than it once was, are more complex than simply a response to a persistent demand from infertile couples. Sociodemographic changes over the past 25 years, which were noted above, may provide more significant explanations for the demand. Aral and Cates, in their often-quoted article in The Journal of the American Medical Association, have observed a number of reasons for an increasing demand for infertility services. 63 One reason is a growing number of infertile couples, although this does not mean that infertility is on the rise but, rather, that a large portion of the population has entered its primary reproductive years. They also point to an increased number of physicians with an interest in infertility, as a result of a decline in demand for obstetrical services, technical improvements in the ability to diagnose and treat infertility and, in the United States in particular, a recognition of the profitability of this area of practice. For example, in his address to the Pacific Coast Obstetrical and Gynecological Society annual meeting in 1989, Dr. Eugene Sandberg is quoted as saying: "The age of specialization is certainly on us and can be found in essentially every field, be it business. academia, or sport. There is little reason to exempt gestation."64

It would appear both that the demand for infertility services is on the rise because the technical expertise is improving *and* that the technology is improving because the demand for services is increasing. It is also clear, however, that the increased focus on the issue of infertility likely has more to do with social explanations for infertility than with any noticeable increase in infertility in the population.

The women's movement, the consumer health movement, and a growing ethic relating to our right to health care services have all contributed to a changing view of infertility. Advances made in making

more options available to women in other areas of their reproductive health (i.e., contraception) have contributed to an expectation that solutions can and will be found for fertility problems.

The Meaning of Choice

The role played by the popular media must not be underestimated in its influence on public perceptions of infertility and new reproductive technologies. A great deal of the popular media coverage on infertility and the new reproductive technologies argues that the (supposed) increase in the problem of infertility is caused in part by STDs and in part by women's decisions to "delay" childbearing: "the decision of some women to wait until the brink of reproductive senility before turning their thoughts to procreation."65 This particular citation from the popular press is an apt illustration of how language can distort reality. Derogatory and misleading phrases like "the brink of reproductive senility" create an unsympathetic portrait of what, for many women, is an ongoing and difficult decision. Many women who have been encouraged to pursue education and careers soon learn that taking time out from either path to have children is viewed with disdain by employers and potential employers. Women with few extended family resources and low-to-moderate incomes also may find adequate and affordable child care in short supply. The notion that women "wait" until they are into their 30s or 40s "before turning their thoughts to procreation" sidesteps the reality that, as social scientist Gina Feldberg recently put it, "it is not easy given the support systems available."66

Scritchfield also notes that a focus on "postponers" as the group most likely to face reproductive problems distracts us from understanding that "the only group for whom infertility seems to be on the rise is 20-24 year olds — a group little affected by decisions to delay childbearing." Indeed, the fact that infertility is more significantly on the rise among younger women (believed to be because of an increase in STDs) than among the women on whom all the attention is focussed is almost completely lost in most media coverage of infertility and the new reproductive technologies.

In addition, the media have played up differences between women's groups and have found that pitting one against another makes for good sales/viewing, as witnessed in the CBC, the *Globe and Mail*, and the *Toronto Star* coverage of the public hearings of the Commission in Toronto in October and November of 1990.⁶⁸ Tensions between some infertile women and some women's groups have often been fuelled by the debate about what constitutes reproductive choice. It has been argued that representatives of some women's groups are being hypocritical when they say women have the right to choose with respect to their reproductive lives and then call for a moratorium or ban on new reproductive technologies. As one woman put it, "We cannot be pro-choice for some and not pro-choice for others." Woolridge draws parallels to a defence of the right to choose to have an abortion even if one personally would not choose to have one. She maintains that a pro-choice position should also advocate for the right

to choose new reproductive technologies even if one would not personally choose to exercise this option. Warren argues that if we are to be true to the notion of pro-choice, this means that we must leave women free to choose even those routes that may be dangerous:

If women's right to reproductive autonomy means anything, it must mean that we are entitled to take some risks with our physical and psychological health, in the attempt to either have or not have children. Neither abortion nor many forms of contraception are entirely safe, but women sometimes reasonably judge that the alternatives are even less desirable. Having a wanted child can be as important a goal as avoiding an unwanted birth.⁷¹

In Canada, the National Action Committee on the Status of Women (NAC) is one of the most publicly criticized women's groups because of its stand on the new reproductive technologies. Judy Rebick, president of NAC, has clarified that NAC's position on the debate is not to ban the technologies completely but rather to call for "a pause, a slowdown, for no new clinics to open until we have clearer data on its success and its safety." She has further argued that the complex questions raised by the new reproductive technologies — Who owns frozen embryos? Do we want to use genetic engineering to create perfect babies? If we support choice in abortion, should we support choice in sex selection clinics? — are not answered with the simple response of "freedom of choice for the individual."

Many critics are calling for more discussion regarding the meaning of choice in reproductive technologies. Rothman claims that we have fought for the right to choose because we believed that it would give women more control and, ultimately, more power. However, the reality is that those who already have the power — physicians — are the ones who have access to the critical information on which many of the key decisions and ultimate choices are made. Canadian lawyer and disability rights activist Sandra Goundry expands on this idea:

The promise of increased freedom to choose is illusory as the medical profession has the power to decide which women are suitable for motherhood, how they will be impregnated, carry the pregnancy and give birth and which foetuses meet their quality control standards. Medical personnel decide which procedures will be used, for what purposes, under what conditions and on whom. Women's control over their bodies becomes attenuated.⁷⁵

Goundry adds that "proponents of the new reproductive technology have (mis)appropriated the language of choice and exploit it for its symbolic value to women." Sandelowski demonstrates how the notion of "a woman's choice" in reproductive matters can be, and has been, used against her, to "blame" her for her infertility:

Infertility is increasingly viewed as an alarming consequence and indictment of our new ability to make reproductive choices. Infertility

has been rediscovered as a disease associated with freedom; specifically with sexual and women's liberation.⁷⁷

The line of thinking to which Sandelowski is referring views women as having, in a sense, "asked for" their infertility, either because they opted for too many sexual partners — which led to a STD — or because they chose education or a career before motherhood — which led to decreased fertility — or both. Scritchfield elaborates on the situation in which many infertile women find themselves:

Women who seek advancement in the world of work are caught in a Catch-22 — they may postpone childbearing to advance professionally, risking diminished reproductive capacity, or they may postpone career agendas for childbearing and substantially detract from career advancements. Either way, women are likely to be held accountable for their choices — either they will be held responsible for any fertility problems that may arise or they will be defined as less committed and less capable professionals because they must turn their attention to the needs of their children.⁷⁸

Infertility is the price they must pay for having sinned "against their nature" (i.e., their role as mothers). While little is publicized about the causes of male infertility (in part because there has been less research on male infertility), research conducted by Woods et al. found that infertile women are often reminded (through the media, by their physicians) that it was choices that *they* made (an intrauterine device [IUD], which led to tubal damage; the birth control pill, which led to ovulation disorders; an abortion, which led to cervical damage) that have led to their infertile state. By exercising their new-found choices, women end up being blamed for the unwanted situation, while male factors and environmental causes of infertility are relatively unresearched.

Sandelowski has aptly chosen the metaphor of "Sophie's Choice" — the dilemma of having to choose between two undesirable alternatives — to describe the situation in which infertile women (and couples) find themselves. The very existence of the technologies to help infertile couples creates a pressure to use them. If the couple chooses not to use the technologies, she argues, this behaviour is viewed as suspect in a pronatalist, pro-technology climate. If the couple chooses to use the technologies, they risk "hardship, the postponement of other life goals, and no cure." She maintains that the reconstruction of infertility as "a disease of choice," or a self-imposed condition, is "no less stigmatizing to those experiencing infertility than earlier moralistic constructions of the disorder." Sandelowski summarizes her thesis:

Infertility emerges as a disease of choice rather than chance because it continues to be prevalent in a time when more control over biological events is being sought and achieved ... Given our new ability to enhance or inhibit fertility, individuals are more likely to be viewed as responsible for the outcome of their reproductive behavior. One consequence of the shift in the burden of responsibility from God or fate to human beings

in the matter of reproduction is that infertile couples are likely to feel more guilty than ever before for their infertility and, therefore, to submit more readily to treatments that are frequently not therapeutic to reduce that guilt.⁸⁴

According to Sandelowski (and others), then, the existence of new reproductive technologies can result in women not only feeling more pressure to try various means to achieve pregnancy, but also living with more guilt if they do not make attempts or if the attempts do not work. Though difficult to measure, this may be a factor contributing to the demand for more services in reproductive technologies. Shattuck and Schwarz clarify the experience of some women this way:

If women are blamed for causing or choosing their infertility, then it should not be difficult to understand why infertile women are demanding and choosing reproductive technologies as a cure for their infertility to alleviate their guilt over lifestyles chosen in the past.⁸⁵

Because some women enter into infertility treatments with this level of conflict and need for resolution, some end up feeling frustrated by the series of interventions that ensues. Menning refers to this as time spent in a "wasteland of suspended animation"; Rehner refers to living with "perpetual uncertainty." Rehner also points out that because there is always something else to try, and the lure of technology is so powerful, women have difficulty in ultimately gaining some relief, which can come from finality, and "they may not even know when it is appropriate to grieve." 88

Menning and followers of the RESOLVE Inc. model of support for the infertile have stressed the importance of grieving. With infertility, Menning noted, one does not grieve the loss of a child but rather the potential loss. The rapid development of new reproductive technologies that has taken place since Menning wrote the first edition of her book has led to a reexamination of the appropriateness of encouraging grieving for infertile women and couples. Unruh and McGrath re-examined the grief model in 1985 and proposed that a more accurate description for most infertile women's experience is one of "chronic sorrow." For women who choose to seek out treatment and do not succeed in achieving a pregnancy, or who have not sought out or choose not to seek out adoption possibilities, the experience of chronic sorrow may more aptly describe their experience. They refer to this as a "functional sorrow" and see it as

a normal response to a life event that seriously jeopardizes women's feelings of self-worth, restricts women's personal ability to feel in control of their lives, compels women to intrusive and sometimes physically painful procedures, and withholds from women the desired child.⁸⁹

We have seen how the pain of infertility can for many be compounded by messages that women have brought the condition upon themselves through choices they have made. The ensuing guilt and frustration caused by this no-win situation may actually contribute to some women's high expectations to have therapies like IVF work for them. These heightened expectations, accompanied by the rapid advancements being made in the field of assisted human reproduction, make it increasingly difficult for women to experience a sense of finality about their infertility.

Infertility as Disability

In addition to the medical profession, the women's movement, and the media, other social forces influence the view of infertility and new reproductive technologies. A change in how society views disabled people, and a growing societal recognition that disabled people are discriminated against and have a right to better access to health and public facilities, appear to be influencing society's view of infertility. The link to the disability rights movement is found in a growing trend toward defining infertility as a disability. Israeli Rachel Levy-Schiff observes that, in Israel, "the infertile woman is seen as physically disabled, a woman in mourning, a tragic figure." Closer to home, Dr. John Jarrell, on behalf of the Society of Obstetricians and Gynaecologists of Canada (SOGC), stated in the Society's brief to the Commission that "the committee recognizes the presence of infertility as a physical handicap which is an appropriate indication for the cautious use of medications to induce ovulation."

Dr. Jarrell has acknowledged that this view of infertility as a disability borrows from the World Health Organization's definition of disability, which

includes the social consequences of a physical impairment.

One of the more impassioned pleas made to the Commission for viewing infertility as a disability was by Karen Woolridge, who has borrowed from the language of disability rights advocates to make her case. She argues that

[i]nfertility must be re-named for what it is: a physical disability. The reproductively disabled should be considered a part of the larger disabled community. The same rights and considerations are due to them as are due to all disabled people. 92

The specific disability, she adds, is that "those who are reproductively disabled are 'dis-able' to perform a physical function: to reproduce." Continuing in this line of reasoning, Woolridge persuasively argues that to deny treatment (in the form of more IVF clinics) to the reproductively disabled would constitute discrimination and make those responsible guilty of "denying health care to the afflicted," which could "contravene the Canadian Charter of Rights and Freedoms." In drawing further parallels with the disability rights movement, she compares the inhumanity of forced sterilization upon the mentally handicapped with the restriction of access to reproductive treatments, which she refers to as "a kind of forced sterilization by neglect."

In contrast, in the submission made to the Commission on behalf of the DisAbled Women's Network (DAWN) Canada — the only Canadian organization devoted solely to the concerns of disabled women — no mention was made of "the reproductively disabled." In fact, in many writings by disabled women published by DAWN (often focussing extensively on prenatal diagnostic techniques in particular), reproductive technologies are looked upon with a great degree of distrust, and disabled women are cautioned to look more closely at what they potentially represent:

These new reproductive technologies are heralded as a triumph of modern science by their proponents. However, in terms of what these reproductive technologies represent for women and persons with disabilities, they are more accurately characterized as potentially the most refined instrument of social control ever made available. ⁹⁶

Woolridge's arguments add testimony to the fact that any universal definition of infertility is elusive. Not only are there varying views as to its categorization — a disability, an illness, a state of being "heart-sick," an indisposition, an unfulfilled desire — but the notion of when one can be classified infertile is also subject to temporal and geographical variations. Is it after one year of regular, unprotected intercourse without achieving pregnancy, as has been the accepted definition in Canada? Is it after five years, as is the case in France? Is it when you "begin to feel concerned that you are not pregnant," as stated in the 1976 edition of *Our Bodies*, *Ourselves*? While medicine scrambles to come up with absolute classifications and definitions, the field is left wide open for interpretation.

Part 2. The Role of the Pharmaceutical Industry in In Vitro Fertilization and Related Assisted Reproductive Techniques

An essential component, perhaps *the most* essential component, of the technologies of IVF and related ARTs is a range of pharmaceutical preparations. They are viewed by some as "miracle drugs," which helped to bring them the baby they so desired, and by others as "hormonal cocktails creating untold harms to women." Some, such as clomiphene citrate, have been on the market for more than 25 years, while others are being used for purposes for which they have not yet received government approval in Canada (such as buserelin acetate, approved in Canada only for use in the treatment of prostatic cancer, but currently used experimentally in infertility treatment). Some even propose that the pharmaceutical industry — not parents desperately seeking a child and not physicians and researchers involved in innovations in the field — is the force that is ultimately leading the movement in new reproductive technologies. Indeed, few could argue against the importance of the industry in this field.

This part will consider some of the key issues related to the pharmaceutical industry's involvement in IVF and ARTs in Canada. It will

begin with an examination of how the industry operates in Canada. It will also look at how physicians learn about the drugs they are prescribing and the marketing techniques used by the industry for products related to women's reproductive health. It will look at the legacy of both assistance and harm done to women through various drugs and devices and how this has influenced the debate on the new reproductive technologies.

It should be noted that this part is not intended to provide a comprehensive overview of the entire role of the pharmaceutical industry in IVF and ARTs. For example, the pharmaceutically funded research in IVF clinics or the under-representation of women in clinical trials for new drugs will not be addressed. Instead, this part will explore specific questions raised in relation to women and reproduction. In this regard, the following remarks, made by Judge Miles W. Lord in 1984 after the approval of a \$4.6 million liability suit against the A.H. Robbins Co., manufacturers of the Dalkon Shield[®] IUD, are relevant:

I dread to think what would have been the consequences if your victims had been men rather than women — women, who seem, through some quirk of our society's mores, to be expected to suffer pain, shame, and humiliation. ... When the time came for these women to make their claims against your company, you attacked their characters. You inquired into their sexual practices and into the identity of their sex partners. You ruined families and reputations and careers in order to intimidate those who would raise their voices against you ...

Your company, in the face of overwhelming evidence, denies its guilt and continues its monstrous mischief ... The only conceivable reasons that you have not recalled this product are that it would hurt your balance sheet and alert women who have already been harmed that you may be liable for their injuries. You have taken the bottom line as your guiding beacon and the low road as your route. That is corporate irresponsibility at its meanest.¹⁰¹

The Pharmaceutical Industry in Canada

While Canada represents less than 2 percent of the world pharmaceutical market, it ranks internationally as the tenth largest consumer of pharmaceutical preparations. The pharmaceutical industry in Canada is composed of 130 companies, consisting of a combination of subsidiaries of larger multinational companies — primarily American, British, and Swiss, representing roughly 80 percent of the industry — and a much smaller number of Canadian-owned firms. ¹⁰² In relation to the global pharmaceutical industry, the subsidiaries of larger companies are relatively small, and the Canadian-owned companies are equally so. ¹⁰³ The majority of companies are situated in Ontario and Quebec, with a greater number in Ontario.

The industry is made up of three kinds of companies. "Innovative" companies are so named because they or their parent companies have researched and developed a product and hold the patent for it. "Generic"

companies produce copies of patented products, having obtained a compulsory licence in order to do so. "Biological companies" produce such products as vaccines, insulin, and blood by-products. (The latter group was not examined for purposes of this paper.) The majority of the innovative companies are represented by the Ottawa-based Pharmaceutical Manufacturers Association of Canada (PMAC), with 66 members, while the generic companies are mostly represented by the Toronto-based Canadian Drug Manufacturers Association (CDMA), with 19 members.

Tensions have long existed between the innovative and generic firms. This problem dates back to the 1920s, when Canada developed a policy related to pharmaceuticals permitting compulsory licences to someone other than the patent holder, thereby allowing them to produce that medicine in exchange for royalty fees to the holder. The Patent Act amendments of 1969 (Bill C-102) further allowed holders of these compulsory licences to import medicines or the active medicinal ingredients of a medicine and to sell the drug domestically. Of concern to the patentholding firms has been the fact that the manufacturers of generics can sell the drug on the market in direct competition with the original drug. One team of industry observers has summarized the situation this way:

Patents have always occupied a quiet but controversial corner of Canadian politics. Patents can be worth millions, so companies fight to get them and once they've got them, they fight to keep them. 105

Following the passage of Bill C-102 in 1969, the multinational patentholding firms began putting pressure (through PMAC) on the federal government to repeal the law, claiming that such competition would make it extremely difficult to keep up the research and development component of their work, and claiming that "thousands of Canadians would die from unsafe generic drugs." Generic firms, with organizations such as the Consumers Association of Canada behind them, argued that they were able to offer the same quality of drugs to the consumer and at a markedly lower cost. In addition, new provincial policies encouraged physicians to substitute the cheaper (generic) product when prescribing. Judy Erola, then Minister of Consumer and Corporate Affairs, commented at the time that "the war got absolutely furious ... the lobbying was, perhaps, I think the strongest lobby I've ever seen."

The result of the flurry around Bill C-102 was the creation of the Eastman Commission of Inquiry on the Pharmaceutical Industry. Its 1985 report recommended, among other things, that new drugs should be awarded a period of exclusivity from generic competition. Amendments to the Patent Act were then made to this effect, and Bill C-22 came into force in December of 1987. In return for this, PMAC agreed to invest \$1.4 billion in research and to create 3 000 new jobs by 1995. With increased patent protection of up to 10 years available to the innovative pharmaceutical firms, considerable concern remained about how this would affect the cost of drugs. To address this concern, Parliament established the Patented

Medicine Prices Review Board, a quasi-judicial body mandated to "ensure that the prices of patented medicines charged by patentees are not excessive." However, compliance with Board regulations is on a voluntary basis.

PMAC's earlier claims that the existing patent legislation was affecting its research and development spending must be considered in light of the type of research that goes on in Canada. As one observer recently noted, "Not since insulin was approved for use in the 1920s has a therapeutic drug been discovered and developed entirely in Canada by a Canadianowned company." 110

The Royal Commission on Health Services (1964) noted that much of the research carried out by Canadian pharmaceutical companies was (and is) "directed toward duplicating already existing drugs." Three types of pharmaceutical research are carried out in Canada: basic research, applied research, and product development. Basic research, which seeks to discover new concepts of drug therapy or totally new drug products, constitutes only 8 percent of all the pharmaceutical research conducted in Canada.

Although efforts are being made to increase the rate of basic research being done in Canada, impassioned claims about the constraints on pharmaceutical research in Canada must be seen in the context of how little truly basic research is currently being carried out in this country.

Profit and the Industry

Even though sales for prescription drugs in Canada in 1990 totalled \$4.4 billion, 115 listings of Canada's top companies by sales will not find many pharmaceutical companies even in the top 100. 116 However, sales are only one measure of a company's importance or success. A more important measure, one in which the pharmaceutical industry is a leader, is in the area of profitability. Within the manufacturing sector in Canada, the pharmaceutical industry "remains among the more profitable." Statistics Canada data comparing 87 manufacturing industries in the 1970s and 1980s found that, by the late 1980s, the pharmaceutical industry ranked number one on two key measures of profitability: rate of return on equity and rate of return on capital employed. (See Tables 1 and 2 at the conclusion of this document.) These data show the pharmaceutical industry to be very stable in Canada and one that consistently attracts the investment dollar.

The industry is able to maintain its profitability, in part, through the lack of price competition and patent protection. Another reason for its success, not often cited in financial literature, stems from the general belief in our culture in the power of medicine and medical solutions. Canadian journalist Ann Walmsley speaks of the prescription drug market as being "recession-proof. Consumers can cut back on restaurant meals, cars and holidays," she adds, "but not on their hypertension medication." In a

revealing interview with a representative from a Manhattan-based research firm specializing in pharmaceuticals, ¹¹⁹ Walmsley elicited the following statement: "For companies that perfect the right remedies, 'it's harvest time.' "¹²⁰ In this example, the company representative is referring to a new product for migraine headache sufferers, which he says will sell for "\$35 a headache."

In the same article, Walmsley further quotes Eric Baker, president of Altamira Capital Corp., a Quebec-based venture capital firm, which invested in a new pharmaceutical company:

Baker [recognizes] that cancer treatments have a potentially huge market. Every year nine million new cancer patients are diagnosed in the world. "Cancer touches most families," Baker says. "So if we can do something for that and get a financial return at the same time, it is like hitting a grand slam home run." 121

The crass notion of making enormous profits at the expense of people's illness is an image that the industry is trying desperately to counteract, and yet it is a reality that must not be ignored. A product manager for a major Canadian pharmaceutical company commented in a 1980 interview to *Maclean's* that his job entailed either "perceiving needs, or creating them" 122

One industry observer commented that the goals of the profession and the industry are in fact at odds:

Most doctors no longer consciously realize that drug companies' goals are diametrically opposed to the goal of the conscientious physician. The drug company can make the largest profit by getting doctors to write lots of prescriptions for their highest priced products. The doctor's goal, on the other hand, should be to prescribe as few drugs as possible, and to use the lowest price effective drug. 123

The industry enjoys its status as the most profitable in the manufacturing sector not only because of patent protection offered to the innovative firms (resulting in decreased competition for a specified period), but because of more complex sociological reasons related to Western society's reliance on medical solutions for health-related problems.

Advertising and the Industry

Many industry representatives are acutely aware of this delicate balance between themselves and the medical profession; on the one hand, responsible physicians do not want to be seen as excessive prescribers of drugs; on the other hand, the industry will remain profitable only if doctors continue to prescribe more and more drugs. They know that if they are to be successful in selling their products, they must use sophisticated marketing techniques. One advertising executive working for the industry referred to the challenge to pharmaceutical companies this way:

Medical men are subject to the same kinds of stress, the same emotional influences as affect the laymen. Physicians have, as part of their self-image, a determined feeling that they are rational and logical, particularly in their choice of pharmaceuticals. The advertiser must appeal to this rational self-image, and at the same time make a deeper appeal to the emotional factors which really influence sales. 124

The industry carries out detailed market research to determine the best methods of selling its products. In a review of the literature on the factors that influence physicians' prescribing habits, researchers found that, although education and consultation with colleagues were important factors, advertising and other marketing tactics of the pharmaceutical industry were particularly significant. In particular, a more recent Canadian review of the issue found that the more heavily a drug is promoted, the more it is prescribed. Dr. Eike-Henner Kluge, Director of the Canadian Medical Association's (CMA) Department of Ethics and Legal Affairs, recently noted that the pharmaceutical industry spends between \$3 billion and \$5 billion annually in North America for advertising and promotion. He added, "These companies are not stupid. They do not spend money on physicians if they do not expect to influence physicians." Its production is the physicians.

One of the more influential ways in which the industry reaches the medical profession is through advertising in medical journals. Indeed, many Canadian journals — a number of which are sent free of charge to every physician in Canada — are heavily subsidized by the industry through pharmaceutical advertising. Canadian physicians are also part of the readership of American and certain European journals, many of which contain a number of advertisements from pharmaceutical companies.

As the number of advertisements appearing in major Canadian medical journals has increased over the past 15 years, it would appear that the publishing industry has been as important to the pharmaceutical industry as the pharmaceutical industry has been to the flourishing of Canadian medical journals.

Case Study: The Bulletin/Journal of the Society of Obstetricians and Gynaecologists of Canada

For a better understanding of the evolution of pharmaceutical advertising in Canadian medical journals pertaining to drugs used in women's reproduction, the author examined the full range of issues of the publication of the SOGC. Although the degree of influence that this publication has over the prescribing habits of Canadian obstetricians and gynaecologists is unknown, it does have a circulation of 30 000 and is one of the few Canadian publications published in its entirety in both French and English. *The Bulletin* is published 10 times a year and is circulated free of charge to all obstetrics/

Case Study (cont'd)

gynaecology (ob/gyn) specialists, ob/gyn residents, family physicians,

and general practitioners across Canada.

The first edition of *The Bulletin* was released in April of 1980 in the form of a three-page foldout bilingual newsletter with an acknowledgment of financial help from Ortho Pharmaceuticals Canada Ltd. and a small (1/4 page) black and white ad from the same company. By 1986, *The Bulletin* had grown to a 16-page publication, still with only one small ad from Ortho. The January-February 1986 issue of *The Bulletin* had changed to a new, glossy format with financial assistance through advertisements from seven pharmaceutical companies. That same year, a six-page ad from Syntex Inc. featured the Synphasic triphasic oral contraceptives. The visual component of this ad consisted of a woman who appears clothed in one shot and nude in another, fingering a string of pearls around her neck. The string of pearls is then used to illustrate the hormonal rises and falls in the menstrual cycle.

By 1987, the number of ads had increased to 12, and the first ad for an infertility drug — Parlodel[®] (Sandoz) — appeared. Coverage of new reproductive technologies increased in 1987, with a special issue on IVF and embryo transfer (IVF-ET) appearing in the spring issue. The drugs Serophene[®], Pergonal[®], Profasi-MP[®], and Metrodin[®] are all manufactured by Serono Laboratories and are reported to have 70 percent of the market sales internationally for human fertility drugs.¹²⁸ Heralding the arrival of Serono to Canada in 1990, the first ad from the company in the June issue reads:

Serono Laboratories provides a full range of therapies that aid conception. And change lives ... Our recombinant technologies will open the way to even greater possibilities for conception ... Serono Laboratories is the world leader in infertility therapy. And we are creating the future.

The appearance of ads concerning drugs related to infertility and IVF accelerated after 1987. The most recent issues in particular contain advertisements for a category of drugs known as LHRH (luteinizing hormone releasing hormone) analogues. These drugs (Suprefact® [buserelin acetate], Lupron® [leuprolide acetate], and Zoladex®) are relatively new and experimental in IVF and ARTs. Interestingly, their approved indications at the time the ads ran were only for the treatment of prostatic cancer. Although the copy for each ad did not specifically endorse using the drugs in infertility treatments, their purpose in a journal of obstetrics and gynaecology would seem to be to influence physicians who are currently using these drugs in IVF and ARTs. This example supports a statement made by Hawkins

Case Study (cont'd)

and Aber in their review of pharmaceutical advertising in 1988, that "advertising appears to create expanded use of certain drugs in cases that physicians might not have considered." Determining the extent to which this statement holds true would require further research.¹³¹

In 1989, the name of *The Bulletin* changed to *The Journal of the Society of Obstetricians and Gynaecologists of Canada*, with publishing now handled by Ribosome Communications in Toronto. Added to the masthead is the phrase "The Official Voice of Reproductive Health Care in Canada." By May 1991, the magazine contained ads from 26 pharmaceutical companies. The most recent issue examined (August 1991) contained 14 pages of pharmaceutical advertisements, 8 pages of monographs related to the drugs advertised, and 63 pages of text. In a short 11 years, the publication has gone from a simple three-page newsletter format with minimal pharmaceutical funding to a glossy, 83-page publication funded for the most part by pharmaceutical companies.

The example of *The Journal of the Society of Obstetricians and Gynaecologists of Canada* and the radical change in its appearance in just over 10 years illustrate the importance of the pharmaceutical industry to the maintenance of certain medical journals and the mechanism for extensive advertising that the journals provide to the pharmaceutical industry.

Another form of industry promotion is through company sales representatives who were formerly called *detail men* but are now more frequently referred to as *product managers*. These representatives visit physicians on a regular basis with information about their new products and with free samples to leave behind. Lexchin has noted that the pharmaceutical companies view their representatives as having a dual role — that of salesperson and educator:

On the one hand they have a commercial function — their goal is to increase the utilization of their companies' products by encouraging physicians to write more prescriptions, but on the other hand, they are also supposed to be educators ... However, there is an obvious potential conflict of interest in the two roles of detailers. Increasing consumption of drugs is not always compatible with better prescribing or better health. 132

One study of Canadian physicians' attitudes toward pharmaceutical representatives reported at the PMAC Annual General Meeting in 1986 found that only 56 percent of physicians considered them to be a credible source of information about drugs. Nonetheless, many physicians rely on pharmaceutical representatives as a source of information about new drugs. Physicians maintain that, with busy schedules and limited time to

attend conferences and keep up to date with the medical literature, a company representative bringing information and samples is a convenient way to find out what is current in the field. Since visits with the physician are very time-limited (usually no more than 10 minutes), it is questionable how strong an educational role the representative can play.

One of the greatest sources of information going directly from the industry to physicians is the Compendium of Pharmaceuticals and Specialities (CPS), published annually by the Canadian Pharmaceutical Association (CPA) and heavily subsidized by the industry. The CPS, published in both French and English, is distributed free of charge to every physician in Canada. 134 Pharmacies, nurses, researchers, and hospitals must purchase the book at a cost of just over \$100. Because it is the only compendial source of drug information in the country and because it is updated on an annual basis, it is the single most widely consulted source of pharmaceutical information by Canadian physicians. Submissions made to the CPS have been prepared by the companies manufacturing the drugs, while other entries are made by the editors. While the CPS may appear comprehensive — because of its sheer bulk — it contains information on less than half of all the pharmaceutical preparations listed in the Canadian Drug Identification Code. Drugs listed in the main body of the text are primarily those of the multinational companies, which can take the time to make submissions, although a more comprehensive undetailed list has been added to more recent editions. The book is also replete with a number of full-page colour advertisements for some of the drugs listed in it, the same advertisements found in medical journals.

A critical analysis of the 1977 edition of the *CPS* was undertaken by Bell and Osterman, who compared the actual submissions to the CPA Guidelines, which were distributed to all manufacturers submitting material to the *CPS*. They found that a substantial proportion of the monographs did not contain the basic subsections recommended by the *CPS* editors, such as overdose symptoms and overdose treatments, and that about one-quarter of the submissions were missing information on side-effects. They also found that the submissions prepared by the manufacturers frequently contained less adequate information than those prepared by the *CPS* editors. While the CPA has addressed some of these shortcomings in more recent editions, Bell and Osterman were harsh in their criticism of earlier editions:

[D]espite claims to impartiality by its editors, the CPS displays a strong bias in favor of the pharmaceutical manufacturers whose products are displayed in its pages ... rather than being the complete, objective source of drug information that the editors claim it to be, the CPS is in fact the paragon of successful drug advertising. Through ready availability, ease of use, annual revision, and pretence to scientific objectivity, the CPS, and as a consequence the pharmaceutical manufacturers, have cornered the market on drug information at the level where it counts the most — the practising physician, nurse, and pharmacist. 136

A less biased source of drug information for Canadian health practitioners is greatly needed. Alternative sources do exist in other countries, such as *Medical Letter on Drugs and Therapeutics* in the United States; however, because of different regulations from country to country, some of the information it contains is not always appropriate for the Canadian market. A relatively small number of Canadian physicians subscribe to *Medical Letter*. 137

The industry is also able to reach physicians by sponsoring continuing medical education courses, conferences, and post-graduate training. The degree of a pharmaceutical firm's involvement in the content of continuing medical education courses and conferences varies from company to company. But unquestionably, a company would not knowingly sponsor a speaker who would in any way hurt the sales of its products, since this would simply be poor business practice. A typical description of the type of funding available from a pharmaceutical company appears in a recent publication of the Ontario Medical Association:

The Upjohn Company supports a wide variety of continuing medical education activities, from sponsoring \$1,000 study awards through the College of Family Physicians of Canada, to planning and supporting medical symposia in subject areas where the company's research efforts are concentrated. Regarding assistance for medical society educational programs, the company will support "visiting professors" to appropriate medical meetings on subjects related to research interest and involvement (italics added). They are also prepared to act as resource people in the organization of medical meetings and continuing medical education programs. In addition, the company makes available an extensive catalogue of medical films for postgraduate training purposes at no charge to the sponsoring association. ¹³⁸

With 30 similar submissions in this same publication, it is evident that the pharmaceutical industry is prepared to give generously to those wishing to avail themselves of this funding. Conscientious physicians or medical educators seeking funds for such activities and not wanting to be beholden to a pharmaceutical company may find themselves in a quandary, since very little funding of a similar nature or for similar functions is available to such a degree from any other industry or from any level of government in Canada.

Companies also assist non-profit organizations devoted to particular health and disability issues. The French-language version of the newsletter of the IAAC, for example, is funded by Serono Canada. Particularly in difficult economic times with government cutbacks to such organizations, some groups face difficult ethical decisions when offered money by pharmaceutical companies. For pharmaceutical companies, it provides an economical and convenient way to bypass physicians and go directly to clients in making their name known. Another means of getting directly to the consumer is by producing public education materials, which are distributed to consumers. Ayerst Laboratories and Ciba-Geigy Self

Medication Products, for example, have both produced pamphlets on menopause, which are available through women's magazines. Both publications offer only a positive portrayal of hormone replacement therapy

in spite of controversies that exist about these therapies.

Some companies also produce educational materials (audio-visual and print) intended for use by both physicians and users of their products. Serono, for example, has produced a series of educational materials about their products intended for use by patients. The author was able to obtain a copy of two of their videos, 139 one on Serophene[®] (clomiphene citrate), the other on Pergonal[®] and Metrodin[®] (human menotropins: FSH and LH gonadotropins), which are shown to couples in infertility programs. An examination of the content of these videos, which are available to Canadian physicians and their patients through Serono Canada, reveals a company that is attempting to present an unbiased portrayal of infertility but that succeeds primarily in convincing the viewer of the importance of its products. The video also uses outdated and sexist images to convey its While both videos acknowledge that the drugs are not completely without risk, the risks that they do acknowledge are minimized. The video for Serophene® points out that a woman can develop enlarged ovaries (ovarian hyperstimulation syndrome¹⁴⁰) as a result of using the drug but that the ovaries usually resume normal size three months after the woman discontinues use. Other side-effects — hot flashes, nausea, blurry vision, headaches, and lower abdominal pain - are said to be "temporary in most cases, and cause no serious problems." It is acknowledged in the medical literature, though not in these videos, that guaranteed evidence of complete safety of clomiphene citrate has not yet been found and that, in particular, the effects on the children born of women who have gone through ovulation induction with this drug have not been fully researched.141

The video on Pergonal® and Metrodin® also acknowledges in the first five minutes of the film that drug treatment for fertility problems can be expensive, time-consuming, and emotionally difficult and can carry a risk of multiple births. The producers are to be congratulated for this honesty but, unfortunately, not for the content that follows. Couples who have been through IVF and drug stimulation are interviewed, with one husband who has learned to give his wife her injections commenting, "You need to take it lightly ... You're looking at your wife's behind and you have the opportunity to inflict some pain ... we had to deal with that." The female reproductive system is compared to a car race — "the Follicle 400" through an animated depiction of eggs in race cars "trying to finish first," with "The pit, short for pituitary, [giving] the signal to start their engines." The eggs are caricatured as females, heavily made up and winking at the camera. Those follicles that do not make it to the finish line are depicted as being in car crashes. The parallel is a clever one and is intended, through its humour, to introduce some levity into a serious subject. But humour can also have the effect of trivializing the subject and of alienating any viewers who do not find that particular brand of humour funny. In this case, the humour also has the effect of minimizing or dulling one's memory to the more serious statements about risks and costs made at the beginning of the film. It is also worth mentioning that, while the primary viewers of these videos are women (as the ones who will ingest these drugs), the producer, director, script writers, and announcer in the film are all men.

The larger question raised by pharmaceutical involvement in continuing education courses, conferences, and educational materials relates to the degree to which that involvement — be it covert or overt — perpetuates the belief in drug solutions for all health problems. As one observer noted:

Although some companies provide excellent educational services, it ought not to be forgotten that drug firms are in business to sell drugs. 142

To what extent does the ready availability of pharmaceutical solutions contribute to what the Quebec Conseil des affaires sociales et de la famille calls "une mentalité médicament" (a pill mentality)?¹⁴³ An underlying concern expressed by many observers of the industry is that the industry is creating or perpetuating a reliance on pharmaceutical solutions at the expense of exploring healthier, less costly, and more appropriate alternatives. For example, research conducted at the Addiction Research Foundation in Ontario found that one-quarter of women in shelters for battered women were taking central nervous system depressants (barbiturates, other sleeping pills, and benzodiazepines) at the time of their stay at the shelter.¹⁴⁴ Are physicians thereby rendering women less able to act on their situation because they are numbed by psychotropic (moodaltering) drugs?

Pharmaceutical promotion also raises questions about the appropriateness of educating physicians in this way. Concern about this issue prompted the CMA to recently adopt a series of strongly worded guidelines on what physicians may or may not accept from pharmaceutical companies. The practice of providing gifts to physicians who attend a company's conference or educational seminar, for example, has been called into question and has been ruled unethical.¹⁴⁵

The industry is clearly aware of the need to clean up its image with respect to advertising, to provide accurate information to consumers, and to carry out research in an ethical manner. PMAC has, over time, engaged the services of a number of consulting and marketing firms to determine how the industry can best reach its "stakeholders" with information about the industry and its products and to help improve its image. One consultant warned that "the industry is under intense scrutiny, even siege, by groups seeking improved product information, alternatives to drugs, and elimination of overprescribing, [and] stereotyped advertisements relating to women." In 1986, PMAC resolved to spend almost \$1 million a year for the following five years in improving its image

with its stakeholders. It was told by one of its consultants that it should "conduct itself with the public interest in mind ... [and] it should develop long-term 'dialogue' with groups whose values the industry might not share." 148

In part, PMAC has been responding to a growing criticism of the industry, which has gained momentum in the past 20 years. The criticism, however, is not new; Oliver Wendell Holmes (1809-1894), Dean of the Harvard Medical School in the mid-nineteenth century, wrote:

If all the drugs in the Pharmacopia, with a few exceptions, were thrown into the sea, it would be better for mankind and the worse for the fishes.¹⁴⁹

Holmes was more prophetic than he may ever have known. In response to an international concern that the industry was producing too many unsafe, unnecessary, and overpriced drugs, the World Health Organization launched its Action Program on Essential Drugs in 1977. The program designated roughly 200 drugs as safe, inexpensive, and of proven therapeutic value, thereby deeming the remainder to be unessential or redundant. This program has been monitored over the past decade by an international watchdog group known as Health Action International (HAI), whose activities also include alerting the public to unsafe drugs and misleading advertising. The Canadian chapter — HAI Canada — was formed in Canada in 1985, with a majority of its members representing women's health organizations.

In summary, we have seen that advertising for the pharmaceutical industry through advertisements placed in medical journals, information and samples distributed by company representatives, the sponsorship of continuing medical education courses for health care professionals, or the funding of publications of non-profit organizations is an important means of distributing information about the industry and its products to both physicians and consumers. At the same time, the industry recognizes a degree of public criticism of its publicity efforts and has taken measures to counteract that criticism.

Women and the Pharmaceutical Industry

In Canada and the United States, women are vital to the sale of pharmaceutical products. Firstly, they consume more drugs than do men, for a variety of complex reasons — some related to women's longevity, some to their reproductive capacities, and some to the medical establishment's inability to find a more appropriate response to women's anxiety and stress. ¹⁵⁰ In addition, women are key players in the distribution of drugs through their roles as health care workers and as mothers, sisters, and daughters. Within families, women are key decision makers with respect to which over-the-counter medications should be given to family members and when. They are also more likely than men to be involved in

interactions with physicians and pharmacists vis-à-vis medication for the family. McDonnell has noted that this role has been largely ignored:

This central role of women in health care has gone largely unnoted, perhaps precisely because it is so universal, so apparently "natural" for women to assume responsibility for the care and healing of others. ¹⁵¹

Women may not receive any outward recognition for this important role, but the industry recognizes the importance of using images of women to market its products. Until very recently, when advertisers discovered that using fathers in advertisements can be a useful attention-getting device, women have traditionally been the key figures used in advertisements for over-the-counter drugs for the entire family, presumably so that women will identify with the women in the ads and ultimately purchase the product.

With respect to prescription drugs, the industry uses those same female images to reach its primary consumers — doctors. As noted above, advertisements for prescription drugs are found in great abundance in a wide variety of medical journals, many of which physicians receive unsolicited and free of charge on a regular basis. A key feature of the advertisements that appear in these journals is that they are intended for use by the prescribers of the drugs - physicians - and they are not generally viewed by the wider public. Over the past 20 years, the industry has come under considerable attack for the way in which it has depicted women in many of its advertisements. Claims that the ads perpetuated sex role stereotypes and that many were blatantly sexist began to appear in the early 1970s. Indeed, some of the most glaring examples of demeaning and sexist advertising appeared in journals in the 1970s. Advertisements for a wide range of products repeatedly depicted women in passive roles and as handmaidens to physicians, husbands, and children. Sexually suggestive ads were common (a phenomenon not unique to the pharmaceutical industry).

One advertisement for Valium[®] (Hoffman-LaRoche) begins with the eye-catching line, "Sally Wilson has lost her reputation." Sally is referred to in the ad copy as "an unpredictable grouch" who was helped only by Valium[®]. A 1975 ad for a laxative, Senokot[®] (Purdue Frederick), catches the reader's eye by using a seductively posed woman in a bikini. Examples abound of women in infantilizing and demeaning postures, often having little or no relationship to the product being advertised.

As early as 1971, an analysis of women in advertising found that four general themes were repeated:

- a woman's place is in the home;
- women do not (and cannot) make important decisions or do important things;
- women are dependent and need men's protection;
- men regard women primarily as sexual objects. 152

While research into the depiction of women in pharmaceutical advertising in the 1970s focussed more on the women in psychotropic drug ads, ¹⁵³ the portrayal of women in advertisements for contraception and other reproductive drugs has captured the interest of researchers in more recent years. ¹⁵⁴ In a review for Health and Welfare Canada of advertisements portraying women in Canadian and American medical journals in the 1970s and early 1980s, Ford found themes similar to those found a decade earlier:

- women cannot cope;
- doctors know best;
- women are dumb;
- women can be a real nuisance to others;
- a woman's biology is her destiny;
- women are a homogeneous group.

A similar analysis of Quebec journals conducted by Guyon and colleagues in 1981 found women over-represented in advertisements for anti-depressants and sleeping pills. 155

A more recent review by Hawkins and Aber in 1988 of the advertisements in key American medical journals found that readers are still being exposed to images of women that are negative and outdated. The authors compared the depiction of women and men in certain roles to actual data on men and women in these positions. The roles they examined were physicians, nurses, other health care professionals, women at home with children, women in the paid labour force, etc. While the researchers found some improvements over advertisements of the 1970s, they found that women were still under-represented as providers of care and over-represented as consumers of care. Men were mostly active, women mostly passive. If women were depicted as under stress, it was usually because of family, housework, and menial tasks; men were stressed by their jobs. Failure, compliance, abuse, and simplicity were found to be recurrent themes, and women in particular were portraved as either not bright enough to follow directions or liable to misuse drugs prescribed for them. 156

The industry has begun to respond to these criticisms regarding its advertising. Women are now found more frequently in positions of control and authority in advertisements, and overtly sexist images have been toned down considerably. But these images have not disappeared completely. Even a cursory review of advertisements from Canadian journals from the past six years revealed images in which women are depicted scantily clad and seductive and as caricatures of frazzled housewives or waitresses.

An analysis of the stereotypical depictions of women in pharmaceutical advertising raises the question of whether such images "merely reflect reality or ... actually influence and shape reality." It raises further questions about how physicians, in turn, see the women they are treating

in their offices, and whether these advertisements influence their prescribing habits. Prather and Fidell summarize the issue this way:

Although it cannot be argued conclusively that advertisements cause physicians to prescribe differently for women and men, one can at least speculate upon the possible effects these advertisements may have upon both patient and physician. ¹⁵⁸

A further concern related to women and the pharmaceutical industry is the lack of involvement that women have in decisions made about the drugs that will affect them. With respect to research carried out on drugs for women, Tudiver notes that

women have no real control over how drug research is formulated, carried out and interpreted, nor do they determine how drugs — including drugs used primarily or solely by women — are marketed and prescribed. Corporate executives and scientists, mostly men, make such decisions. 159

The operative phrase in Tudiver's analysis is "real control." It has been argued that there are signs of progress, since more and more women are being hired in the pharmaceutical industry, as in many other manufacturing industries. Even by the industry's own admission, most women are only at entry-level positions and have difficulty moving up the ladder to key decision-making positions. ¹⁶⁰ It remains to be seen whether women in more senior positions in the pharmaceutical industry would have any real impact on the problem of sexist advertising. An additional factor compounding women's involvement in decision making and control is the problem of attracting more young women into the field of scientific research.

Further complicating any real possibility of women's voices being heard in discussions related to drug research on women is the fact that much of the key research related to women's health is conducted by the parent companies of the larger firms, most of which are located outside Canada.

While they are only one measure of a company's integrity, advertisements in medical journals take on a symbolic importance. Can a pharmaceutical company that continues to use outdated images of women to advertise its products view women within its own company as equals? What influence do these images have on how physicians view not only their female patients but their female colleagues? As more consumers and physicians scrutinize the ads found in medical journals, the industry struggles to improve its image and to respond to concerns.

Reproductive Drugs and the Pharmaceutical Industry

In addition to being the dominant consumers of a number of categories of drugs, women receive almost all of the prescriptions for drugs related to reproduction. ¹⁶¹ These include various forms of contraception, hormone

replacement therapy for menopausal symptoms, and drugs used for infertility. In 1988, hormones rated as the sixth highest category of drugs prescribed in Canada, constituting a market share of 6 percent. "Sex hormones" and "other hormones" are experiencing one of the highest rates of growth of all categories of prescription drugs in Canada. 162

Since the synthesis of estrogen in the 1930s and the discovery of its effect on the pituitary gland, synthetic hormones have had an impressive, though rocky, history in the annals of the pharmaceutical industry. Unaware either that hormone preparations could cross the placental barrier and cause harm to the fetus, or that they had potentially carcinogenic 5-effects on women who took them, pharmaceutical companies marketed these preparations in the 1940s and 1950s for prevention of miscarriage, to enhance fertility, and to alleviate the discomforts of menopause. Animal research from this same period linked the use of both synthetic and natural estrogens with higher risks of cancer.

By the mid-1950s, discoveries leading to the development of an oral contraceptive were under way. Testing of the forerunner of today's contraceptive pill - consisting of large doses of both estrogens and progestins — were carried out on Puerto Rican and Haitian women in the late 1950s. In 1960, the Federal Drug Administration (FDA) in the United States approved the first oral contraceptive pill, on which basis was begun "the first mass prescription in medical history of a non-medical drug." 163 The FDA chose to minimize concerns about blood clotting, which had been raised during the trials, and it was not until 1969, following more extensive testing on a large sample of women in Britain, that a warning to this effect (to pharmacists and doctors, not to patients) was issued. As research continued throughout the 1970s, women slowly learned that heart disease, hypertension, and stroke were significantly more common in Pill-users than in non-users. Questions relating to a link to cancer were also being raised. Epstein refers to the worldwide use of the Pill as "the largest uncontrolled experiment in human carcinogenesis ever undertaken" and attributes this to "the importunity of the drug industry; in its massive marketing and heavy promotional campaigns for a poorly tested product and its unwillingness to face substantive questions on risk of cancer and cardiovascular disease that subsequently developed."164 Although its problematic legacy is still with us today, the Pill has nonetheless afforded millions of women worldwide a degree of control over their reproduction that is historically unprecedented.

Case Study: DES

If reference is made to harms caused by drugs taken in pregnancy or to dangerous drugs generally, thalidomide is the most frequent example cited. This is understandable, since the visual effects of thalidomide damage — missing or stunted limbs — are not easily

Case Study (cont'd)

forgotten and elicit immediate sympathy. 165 Both improperly tested and aggressively marketed, the drug was given to pregnant women for a brief period in the 1960s to prevent nausea. It was withdrawn from the market when its effect on the offspring was discovered. It had been on the market in Canada for only 11 months but was used extensively on Canadian Forces bases in Europe.

Because DES was usually given early in a pregnancy and at a time when the reproductive organs were forming, the most significant harms to the offspring have been related to their reproductive organs. In daughters, problems range from a rare form of vaginal and cervical cancer to a host of structural irregularities linked to problems conceiving and carrying a pregnancy to term. Sons also have problems, including a higher incidence of testicular abnormalities and fertility problems. Further, in 1984, a major study of DES mothers showed a higher incidence of breast cancer in middle age. 166

In Boston in the early 1970s, a cluster of very young women developed a rare form of vaginal cancer that, until that time, had been found almost exclusively in post-menopausal women. A mother of one of the young women innocently inquired whether the drug she had taken during her pregnancy with this daughter might have anything to do with her daughter's cancer. Her inquiry proved to have an impact she could never have predicted. Investigation into the backgrounds of this group of women found substantial proof that most of them were the daughters of women who had taken DES during pregnancy. Very soon after, the drug was banned for use in pregnancy in the United States; Canada followed suit in 1971. After its ban for use in pregnancy in North America, the manufacturers of DES continued to market it in developing countries; reportedly, it is still being prescribed for use in pregnancy in some countries, in spite of international warnings since the 1970s. 167

The full range of harms to the reproductive or other body systems is not yet known, and laboratory research consistently shows that the effects of exposure to DES continue throughout the lifespan of the DES-exposed offspring. For example, animal research in the 1980s showed evidence of impaired immune systems and a higher incidence of autoimmune disease. Astonishingly, ongoing research into the full effects of exposure to DES is "insecure and inconsistent" at best. ¹⁶⁸ No major follow-up research projects are known to be going on in Canada at present, in spite of an available population of an estimated 500 000 DES-exposed people. ¹⁶⁹ The DES Research Registry, established at the Wellesley Hospital in Toronto in 1985, lasted a brief two years and has been inactive since its funding was not renewed.

Case Study (cont'd)

Margaret Lee Braun, one of several hundred DES daughters diagnosed with the rare form of DES-related vaginal cancer in her early 20s, recently summarized the experience of the DES-exposed to the Office of Research on Women's Health in the United States:

Today, as I face you, my injuries, like the injuries of all DES-exposed, are invisible — but a constant in my life. I represent three generations of Americans who are hurt, scared and scarred by a toxic prescription drug. I represent the DES daughters who suffer repeated miscarriages, often at five and six months into their pregnancies. I represent the DES mothers who despair over their innocent decision, 20-to-50 years ago, to take a drug prescribed by their doctor. Who wonder if they will have grandchildren. I represent the young women, diagnosed with clear-cell cancer in their early 20s, whose entry to womanhood is marked by the removal of their vagina and reproductive organs. I represent the DES sons who don't know what to expect as they age. I represent the hundreds of thousands of DES-exposed people all over the world who rely on the research in this country to educate their governments and their physicians. 170

The story of DES remains an example of how well-intentioned physicians can prescribe a drug to trusting women, only to learn the consequences decades later. Ironically, it is a medical and pharmaceutical mistake that has created a large group of women with fertility problems, many of whom have, in turn, become dependent on pharmaceutical solutions to their problems.

When the DES example is cited in discussions of drugs currently being used in IVF and ARTs, critics are frequently reminded that the process of drug approval in Canada has tightened up considerably since the days of DES, and that a drug such as DES for use in pregnancy would never make it through the approval stages today. However, although they are not all hormone preparations, the drugs used in IVF and ARTs are on the same trajectory as the drugs described here. The woman being prescribed these drugs may ask a few more questions than did her 1950 counterpart being prescribed DES, but she often shares that same degree of faith in her physician in the hope that this drug will help her to obtain what she most wants -- a live, healthy baby. While today's drugs have been through more rigorous testing than DES and the first versions of the birth control pill, the jury is still out on the long-term effects on the women who take them and on the effects, if any, on their offspring. Of the key drugs used in IVF and ARTs, only one - clomiphene citrate, introduced in 1967 - has been on the market for more than 20 years. In his presentation to the Royal Commission on New Reproductive Technologies on behalf of the SOGC

Subcommittee on Drugs and the New Reproductive Technologies, Dr. John Jarrell of the Department of Obstetrics and Gynaecology at the University of Calgary noted that

the long term effects of the vast majority of drugs on the fetus are completely unknown and when presented with a situation in which the use of these drugs is being considered, therapy is instituted on the basis of risk versus benefit and the severity of the medical situation of the mother. 171

In spite of the comment by one product manager of a major Canadian pharmaceutical company (who wished to remain anonymous) that "pharmaceutical companies are getting out of the business of reproductive drugs because of the high rate of litigation," it is clear that for some companies, the new reproductive technologies represent a lucrative field of endeavour. Serono Canada, now currently involved more than any other Canadian company in the area of assisted human reproduction, foresees continuing in women's reproductive health with the proposed introduction over the next few years of therapies for menopausal disorders. 173

One of the few companies to make a submission to the Commission stated that it felt an "obligation to make these procedures and products available to Canadians who wish to explore all options [and that by] failing to do so, not only do we convey a lack of compassion, we fall behind other countries in an effort to assist infertile couples in their quest for children." Perhaps the most significant commentary on where we can expect to see the market for fertility drugs heading over the next decade comes from Serono Canada. The 1990 Annual Report of the Ares Serono Group states that "the global human fertility market is worth approximately half a billion dollars, with strong growth projected through the end of the century." 175

Pharmaceutical companies are well aware of the complex social and ethical issues related to new reproductive technologies, and in the name of good business they should be concerned about these issues. In a brief presented to the Commission by Organon Canada Ltd. (a Canadian subsidiary of the Dutch company, Organon International, with a long history of research and development in hormones and fertility-related drugs) the authors refer to the "politicization of in vitro fertilization" as a key issue in this field. However, while aware of the debates, Organon does not come to the same conclusions as do many ethicists and social scientists. The Organon brief points to the Australian example in which "Gallup Polls ... have repeatedly indicated that the majority of the population ... are in favour of in-vitro fertilization" and concludes from this that "there would seem to be no reason to restrict availability for either public or private patients on ethical or social grounds." It points to "discriminatory regulations and legislation" as the stumbling block to further expansion of IVF in Australia. As regulations and legislation are established in Canada, we can no doubt anticipate that pharmaceutical companies who stand to gain from the proliferation of IVF clinics will, similarly, see such regulatory measures as stumbling blocks.

With the exception of Serono Canada, whose livelihood depends in large part on the sale of drugs related to IVF and ARTs, the success or failure of most of the pharmaceutical companies involved in this field does not depend on the sales of fertility-related drugs. For example, Parlodel® (bromocriptine) represents only 12 percent of Sandoz's total sales. ¹⁷⁶ Nonetheless, given the rapid pace at which this field is growing and the strong influence that the industry can have on physicians working in this area, those concerned about the impact of the new reproductive technologies on women would be wise to monitor the field and the trends within it.

Conclusion

Although expanding at a rapid pace, IVF and ARTs are, historically speaking, still in their nascent years. Pharmaceutical preparations play an important role in these technologies, and the continuance of these technologies is in part dependent on developments in the pharmaceutical field. Hence, an examination of the pharmaceutical industry and its role in this area is an important task of the Commission. As the primary recipients of the drugs, women, and their relation to the pharmaceutical industry, are equally important areas of examination.

We have seen that the pharmaceutical industry is a thriving and profitable one in Canada. With the exception of one company, Serono Canada, drugs related to infertility and ARTs are not a major contributor to the industry's currently healthy state, although other drugs intended for women's reproductive health are not an insignificant contributor to that level of profit. The legacy left behind by drugs like DES and devices such as the Dalkon Shield® have led some companies to believe that getting out of the business of products for women's reproductive health is the best solution; for others, this line of products may represent the key to their future success.

We have also seen that the means by which the industry disseminates information about its products have repeatedly been called into question by industry critics over the years. The often derogatory depiction of women in much industry advertising in medical journals raises questions about the industry's integrity in its concern for women. Further, the industry's heavy investment in sponsoring conferences and continuing medical education for health professionals has raised concerns about the less than neutral fashion in which physicians learn about drugs. To its credit, the pharmaceutical industry has made many attempts to rectify negative images and questionable practices in marketing its products. Because the potential for abuse and harm in the area of new reproductive technologies is high, critics of the industry will continue to watch developments closely.

Glossary

Analogue: "A chemical compound having a structure similar to that of another but differing from it in respect to a certain component; it may have similar or opposite action metabolically." (*Dorland's Pocket Medical Dictionary*, 23rd ed., 1982)

ARTs (Assisted Reproductive Techniques): This is a general term used to describe a wide array of techniques used to assist women in conceiving. It includes in vitro fertilization; embryo transfer; gamete intrafallopian transfer; artificial insemination; freezing of eggs, sperm, and embryo; sperm micromanipulation; and the pharmaceutical preparations used in most of these techniques.

Etiology: The science dealing with causes of diseases.

Generic Product: "A pharmaceutical product which is a copy (i.e., the same active ingredients, strength and dosage form) of a brand name drug product. Generic copies of patented medicines are generally marketed under a compulsory licence." (Patented Medicine Prices Review Board)

Infertility: This term is generally used (and is used in this document) to describe the inability of a woman or a couple to achieve a pregnancy after a determined period of unprotected sexual intercourse; definition of the length of this period varies internationally. It can also refer to the inability of a woman to carry a pregnancy to live birth.

In Vitro Fertilization (IVF): (In vitro = in glass) A procedure in which an egg is surgically removed from a ripe follicle and fertilized by a sperm cell in a protected environment outside the human body. After growing in the protected environment for about two days, the fertilized egg is (usually) returned to the uterus of the woman who produced the egg, in order to gestate.

Licence, Compulsory: "A licence granted by the Commissioner of Patents that permits the licensee to import, make, use or sell a patented invention pertaining to a medicine. The compulsory licensee pays licence fees or royalties to the patent holder for use of the patented invention." (Patented Medicine Prices Review Board) Licence, Voluntary: "A contractual agreement between the patent holder and a licensee under which the latter is permitted to exploit a patented invention, usually for some consideration paid to the patent holder." (Patented Medicine Prices Review Board)

Male Factor Infertility: A term used to describe infertility where the cause stems from the man. Causes include deficiencies in sperm production, blockage of the sperm delivery system, injury to or malformation of the testicle, disorders related to hormone production, undescended testes, or the presence of a varicose vein around the testicle (varicocele).

Medicalization: The process by which behaviours or conditions are given medical meaning, defined in terms of health and illness.

Patent: "A monopoly limited in time, granted by the state for a new invention. A patent gives the patentee the exclusive right to make, sell or otherwise exploit the invention." (Patented Medicine Prices Review Board) Further distinction is made between a **product patent** — when the actual drug is patented — and a **process patent** — when the process by which the drug is made is patented. In Canada, only process patents are issued.

Post-Partum: The period after childbirth.

Pro-Natalism: Any attitude or policy that is "pro-birth," that encourages reproduction, that exalts the role of parenthood.

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Side-Effects: In the context of this document, used to describe short-term and long-term adverse reactions to a drug.

Women's Health Movement: A social movement that has as its primary goal the reclaiming of knowledge about and control over women's bodies.

Table 1. Rate of Return on Capital Employed, Before Taxes, 1977-1986

Year	Pharmaceutical industry	All manufacturing	Rank of pharmaceutical industry, out of 87 manufacturing industries
	(Perc	ent)	
1977	18.7	10.8	13
1978	20.4	12.8	12
1979	24.9	16.2	10
1980	27.1	14.7	4
1981	27.8	11.9	1
1982	27.1	3.6	2
1983	31.5	6.7	1
1984	37.2	11.0	3
1985	38.4	9.1	1
1985	38.4	9.1	1
1986	41.4	10.7	1
Average	29.5	10.8	5

Source: Canada, Statistics Canada, *Corporation Financial Statistics* (Ottawa: Minister of Industry, Science and Technology, various years).

Table 2. Rate of Return on Equity, Before Taxes, 1972-1986

Year	Pharmaceutical industry	All manufacturing	Rank of pharmaceutical industry, out of 87 manufacturing industries
	(Perc	cent)	
1972	24.7	14.1	8
1973	24.3	19.7	17
1974	27.3	22.8	19

Table 2. (co	ont'd)
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Year	Pharmaceutical industry	All manufacturing	Rank of pharmaceutical industry, out of 87 manufacturing industries			
	(Percent)					
1975	25.0	17.8	12			
1976	. 22.7	15.8	15			
1977	21.4	14.7	16			
1978	22.7	17.4	20			
1979	28.3	21.9	17			
1980	30.1	20.1	10			
1981	31.0	17.4	6			
1982	30.0	5.4	7			
1983	33.9	9.9	3			
1984	40.3	15.7	2			
1985	41.1	12.7	3			
1986	45.4	14.9	1			

Source: Canada, Statistics Canada, *Corporation Financial Statistics* (Ottawa: Minister of Industry, Science and Technology, various years).

Notes

- 1. N. Pfeffer, "The Hidden Pathology of the Male Reproductive System," in *The Sexual Politics of Reproduction*, ed. H. Homans (Aldershot: Gower, 1985), 44.
- 2. "A Royal Commission on New Reproductive Technologies: The Mandate" [press release], Ottawa, Office of the Prime Minister, 24 October 1989.
- 3. D.E. Nye, Electrifying America: Social Meanings of a New Technology, 1880-1940 (Cambridge: MIT Press, 1991).
- 4. U.S. Congress, Office of Technology Assessment, *Infertility: Medical and Social Choices* (Washington, DC: U.S. Government Printing Office, 1988), 3.
- 5. L. Vandelac with the collaboration of M. De Koninck, "Des technologies de reproduction à l'industrie du vivant," in Reproductive Technologies and Women: A Research Tool/Femmes et technologies de procréation: Outils de recherches, ed. CRIAW/ICREF Working Group on Reproductive Technologies (Ottawa: CRIAW/ICREF, 1989), 83.

- 6. The impact of feminist discourse was in evidence during the public hearings phase of the Royal Commission on New Reproductive Technologies, when many individual women and couples with fertility problems made reference to feminist works during their deputations sometimes in agreement with the criticisms, sometimes not.
- 7. S.O. Aral and W. Cates, Jr., "The Increasing Concern with Infertility: Why Now?" *JAMA* 250 (1983), 2327-31; P.M. McShane, "In Vitro Fertilization, GIFT and Related Technologies: Hope in a Test Tube," *Women and Health* 13 (1-2)(1987), 31-46; M. Sandelowski, "Sophie's Choice: A Metaphor for Infertility," *Health Care for Women International* 7 (1986), 439-53; S.A. Scritchfield, "The Social Construction of Infertility: From Private Matter to Social Concern," in *Images of Issues: Typtfying Contemporary Social Problems*, ed. J. Best (New York: Aldine de Gruyter, 1989), 99-114.
- 8. This shortcoming was noted by Doctors Mosher and Pratt at a meeting with Commission staff in Ottawa on 2 August 1991. They commented that "the topic has been a relatively minor one" until recently.
- 9. W.D. Mosher and W.F. Pratt, Fecundity and Infertility in the United States, 1965-1988, Advance Data from Vital and Health Statistics of the National Center for Health Statistics, No. 192 (Hyattsville: U.S. Department of Health and Human Services, 1990), 4; T.R. Balakrishnan, E. Lapierre-Adamcyk, and K.J. Krótki, Family and Childbearing in Canada: A Demographic Analysis (Toronto: University of Toronto Press, 1993); U.S. Congress, Infertility, 50.
- 10. Exploratory research conducted for the Canadian Foundation for Women's Health Care in 1988 found through focus groups with women in a wide range of ages that "magazines and other forms of print are seen as good sources of information." Exploratory Research: Canadian Women and Their Health Care (Toronto: Informa, 1989), 14.
- 11. The French-language version of *Homemaker's Femme au foyer —* has a considerably smaller readership and circulation than the Quebec-based *Châtelaine*, and for this reason it was not considered in this examination.
- 12. Back issues of *Homemaker's* magazine between January 1968 and April 1975 were not to be found in the Toronto public or university library systems.
- 13. Information on circulation and the gender breakdown of readership was obtained from the Print Measurement Bureau, whose statistics are based on 1991 research.
- 14. In this context, it is worth noting that rates of performing hysterectomies in the province of Quebec are among the highest in the country.
- 15. The masthead for the Association's newsletter, *Infertility Awareness*, describes the organization as "a national charitable organization offering assistance, support and education to individuals with fertility concerns."
- 16. B.E. Menning, Infertility: A Guide for the Childless Couple, 2d ed. (New York: Prentice-Hall, 1988), xviii.
- 17. Ibid., xiii.
- 18. Ibid., 139.
- 19. Ibid., 83.

- 20. Ibid., xiv.
- 21. Infertility Awareness Association of Canada, *Infertility Awareness* 6 (March-April 1990), 1.
- 22. Infertility Awareness Association of Canada, Testimony before the Royal Commission on New Reproductive Technologies, Ottawa, 18 September 1990, 181-84.
- 23. A decision was made to examine closely this American publication because its three editions provide an historical perspective on changing views, and because the book has enjoyed tremendous success in both English and French Canada (a French edition, *Notre corps, nous-mêmes*, appeared in 1977). There is no comparable Canadian publication that can make these claims. (*Healthsharing* magazine, publishing since 1979, is available only in English; The Women's Health Booklet of the Vancouver Women's Health Collective (1972) is also available only in English and has not had subsequent printings, although the Collective has produced a highly readable resource on infertility: *Infertility: Problems Getting Pregnant* (1989).)
- 24. K. McDonnell, "The Women's Health Movement," in *The Healthsharing Book: Resources for Canadian Women*, ed. K. McDonnell and M. Valverde (Toronto: Women's Press, 1985), 18. For a more detailed (although now somewhat dated) discussion of the Women's Health Movement, see "Le mouvement de santé des femmes," in *Essat sur la santé des femmes*, ed. M. De Koninck, F. Saillant, and L. Dunnigan (Quebec: Conseil du statut de la femme, 1983), 225-67.
- 25. S.B. Ruzek, *The Women's Health Movement: Feminist Alternatives to Medical Control* (New York: Praeger, 1978), 32-33. Earlier versions of the pamphlet had gone through 11 printings prior to turning over distribution rights to Simon and Schuster in 1971. When the Health Book Collective put out its second edition in 1976, the first Simon and Schuster edition had sold over one million copies.
- 26. Boston Women's Health Book Collective, *Our Bodies, Ourselves* (New York: Simon and Schuster, 1971), 86.
- 27. Ibid., 84.
- 28. A.A. Unruh and P.J. McGrath, "The Psychology of Female Infertility: Toward a New Perspective," *Health Care for Women International* 6 (1985), 370.
- 29. Ibid., 371.
- 30. L.S. Williams, "No Relief Until the End: The Physical and Emotional Costs of In Vitro Fertilization," in *The Future of Human Reproduction*, ed. C. Overall (Toronto: Women's Press, 1989), 134.
- 31. Boston Women's Health Book Collective, *Our Bodies, Ourselves*, 2d ed. (New York: Simon and Schuster, 1976), 321.
- 32. Ibid.
- 33. Ibid., 318.
- 34. A statement such as this must be understood in its proper context. One of the main tenets of the women's health movement and a motivating factor behind much of the style of writing in *Our Bodies, Ourselves* is that women know their bodies best, and therefore they must be believed when they speak about their health concerns. An attempt to redress the many years of not having been believed

(concerns relating to menopause, isolation in the post-partum period, the discomfort of PMS, etc.) lies behind statements such as these.

- 35. L.S. Williams, "Wanting Children Badly: An Exploratory Study of the Parenthood Motivation of Couples Seeking In Vitro Fertilization," Ph.D. dissertation, University of Toronto, 1988, 7, note 4.
- 36. Both an advantage and a disadvantage of the writing in *Our Bodies*, *Ourselves* is that each chapter is authored by a different person. Consequently, perspectives on or philosophical orientations to the same issue can vary and even be contradictory from chapter to chapter. Hence, the opinion on new reproductive technologies is far more critical in the chapter of the same title than in the chapter on infertility.
- 37. The term "Luddite" is used to refer to opposition to new technology and is based on the case of a group of workers in mid-nineteenth-century England who attacked and destroyed weaving machines being introduced in their shops because of concerns that they would take away their jobs or reduce the wages of workers.
- 38. G.O. Mellow, "Sustaining Our Organizations: Feminist Health Activism in an Age of Technology," in *Healing Technology: Feminist Perspectives*, ed. K. Strother Ratcliff et al. (Ann Arbor: University of Michigan Press, 1989), 377.
- 39. Infertility Awareness Association of Canada, Infertility Awareness 1 (2)(1985), 4.
- 40. Boston Women's Health Book Collective, *The New Our Bodies, Ourselves* (New York: Simon and Schuster, 1984), 317-23.
- 41. P. Shaw, M. Johnston, and R. Shaw, "Counselling Needs, Emotional and Relationship Problems in Couples Awaiting IVF," *Journal of Psychosomatic Obstetrics and Gynaecology* 9 (1988), 178-79.
- 42. Vancouver Infertility Peer Support Group, Testimony before the Royal Commission on New Reproductive Technologies, Vancouver, 26 November 1990, 341-42.
- 43. F.M. Andrews, A. Abbey, and L.J. Halman, "Psychosocial Factors and Infertility: How Different Are Fertility-Problem Couples from Other Couples?" Synopsis of presentation to the 47th Annual Meeting of the Society of Obstetricians and Gynaecologists of Canada, Toronto, June 1991.
- 44. J. Wright et al., "Psychosocial Distress and Infertility: Men and Women Respond Differently," Fertility and Sterility 55 (1991), 100.
- 45. Ibid., 105-106.
- 46. Pfeffer, "The Hidden Pathology," 31.
- 47. Ibid., 32.
- 48. J. Collins, E. Burrows, and A. Willan, "Infertile Couples and Their Treatment in Canadian Academic Infertility Clinics," in *Treatment of Infertility: Current Practices and Psychological Implications*, vol. 10 of the research studies of the Royal Commission on New Reproductive Technologies (Ottawa: Minister of Supply and Services Canada, 1993).
- 49. Ibid.
- 50. R. Achilles, "Desperately Seeking Babies: New Technologies of Hope and Despair," in Delivering Motherhood: Maternal Ideologies and Practices in the 19th and

- 20th Centurtes, ed. K. Arnup, A. Lévesque, and R.R. Pierson (London: Routledge, 1990), 287.
- 51. A thorough discussion of why the motherhood imperative has held on tenaciously is beyond the scope of this paper. For more on this, see Williams, "Wanting Children Badly."
- 52. L. Koch, "Not Just Eggs but Human Beings," in *Infertility: Women Speak Out About Their Experiences of Reproductive Medicine*, ed. R.D. Klein (London: Pandora Press, 1989), 103.
- 53. Cited in E.B. Brody, "Culture, Reproductive Technology and Women's Rights: An Intergovernmental Perspective," *Journal of Psychosomatic Obstetrics and Gynaecology* 9 (1988), 201.
- 54. Not all women, of course, feel such a sense of control. Birth control still fails, and many Canadian women are prohibited from using birth control or abortion (or choose not to) for religious and cultural reasons.
- 55. Menning, Childless Couple, 3.
- 56. A. Goldman, "The Production of Eggs and the Will of God," in *Infertility: Women Speak Out About Their Experiences of Reproductive Medicine*, ed. R.D. Klein (London: Pandora Press, 1989), 73.
- 57. Merrilyn McDonald-Grandin, quoted in J. Rehner, *Infertility: Old Myths, New Meanings* (Toronto: Second Story Press, 1989), 51.
- 58. Boston Women's Health Book Collective, The New Our Bodies, Ourselves, 420.
- 59. A range of reasons has been proposed for medicine's interest in moving into the area of infertility. Sandelowski offers this summary: "Several factors, including a falling birth rate, the increased emphasis on demedicalized childbirth, and increasing competition from other health care providers in the childbirth domain, as well as a projected oversupply of physicians in general, have created the need for physicians to expand the areas of medical care, to sub-specialize, and to 'assimilate' whatever 'seems to belong' to gynaecologists ... placing infertility squarely within the medical paradigm of diagnosis and therapy allows physicians to expand their patient pool." Sandelowski, "Sophie's Choice," 448.
- 60. Examples that have received the greatest public attention include thalidomide, DES, and the Dalkon Shield $^{\circ}$ IUD. (See more on this in the section on pharmaceuticals.)
- 61. Rehner, Old Myths, 84.
- 62. Cited in K. Banks, "Baby Chase," Equinox 57 (May-June 1991), 78.
- 63. Aral and Cates, "The Increasing Concern with Infertility."
- 64. E.C. Sandberg, "Only an Attitude Away: The Potential of Reproductive Surrogacy," American Journal of Obstetrics and Gynecology 160 (1989), 1446.
- 65. Banks, "Baby Chase," 78, 81.
- 66. G. Feldberg quoted in A. Mitchell, "Postponing Pregnancy Is the Trend ... and It Carries Special Risks," *Globe and Matl* (8 July 1991), A1, A5.
- 67. Scritchfield, "The Social Construction of Infertility," 109.

- 68. M. Landsberg, "Let's Not Rush into Test-Tube Reproduction," *Toronto Star* (2 November 1990); J. Cameron, "Fighting Infertility: Please Respect My Choice," *Globe and Mail* (5 November 1990); S. Rappolt, "NAC Contradictory on Women's Rights," *Globe and Mail* (10 November 1990); J. Rebick, "NAC's Stand on Reproductive Choices," *Toronto Star* (26 November 1990); J. Rebick, "Fifth Column: Feedback," *Globe and Mail* (21 June 1991).
- 69. K. Woolridge, "Caring for the Reproductively-Disabled," Submission to the Royal Commission on New Reproductive Technologies, Toronto, 1990, 12.
- 70. Ibid.
- 71. M.A. Warren, "IVF and Women's Interests: An Analysis of Feminist Concerns," *Bioethics* 2 (1)(1988), 39.
- 72. Rebick, "NAC's Stand."
- 73. Rebick, "Fifth Column."
- 74. B.K. Rothman, "The Meanings of Choice in Reproductive Technology," in *Test-Tube Women: What Future for Motherhood?* ed. R. Arditti, R.D. Klein, and S. Minden (London: Pandora Press, 1984), 23.
- 75. S. Goundry, "The New Reproductive Technology: Triumph of Modern Science for Some, Threat to Equality Goals of Many," in *Four Discussion Papers on New Reproductive Technologies*, prepared by Canadian Disability Rights Council and DisAbled Women's Network Canada, Winnipeg and Toronto, 1990, 55.
- 76. Ibid., 50.
- 77. Sandelowski, "Sophie's Choice," 440.
- 78. Scritchfield, "The Social Construction of Infertility," 110.
- 79. Sandelowski, "Sophie's Choice," 444. A similar type of reasoning has been used by fundamentalist Christians to blame homosexuals for having acquired immunodeficiency syndrome (AIDS).
- 80. N.F. Woods, E. Olshansky, and M.A. Draye, "Infertility: Women's Experiences," *Health Care for Women International* 12 (1991), 186.
- 81. The tendency to blame women and their lifestyle choices for their infertility is not a recent trend; an historical overview of infertility undertaken for this Commission found that similar thinking dates back to the late nineteenth and early twentieth centuries.
- 82. Sandelowski, "Sophie's Choice," 449.
- 83. Ibid.
- 84. Ibid., 442.
- 85. J.C. Shattuck and K.K. Schwarz, "Walking the Line Between Feminism and Infertility: Implications for Nursing, Medicine and Patient Care," *Health Care for Women International* 12 (1991), 334.
- 86. Menning, Childless Couple, 139.
- 87. Rehner, Old Myths, 12.
- 88. Ibid.
- 89. Unruh and McGrath, "Psychology," 379.

- 90. Quoted in A. Solomon, "Infertility as Crisis: Coping, Surviving and Thriving," in *Infertility: Women Speak Out About Their Experiences of Reproductive Medicine*, ed. R.D. Klein (London: Pandora Press, 1989), 181.
- 91. J. Jarrell, Society of Obstetricians and Gynaecologists of Canada, Testimony before the Royal Commission on New Reproductive Technologies, Victoria, 29 November 1990, 120.
- 92. Woolridge, "Caring," 3.
- 93. Ibid., 4.
- 94. Ibid., 3.
- 95. Ibid., 10.
- 96. Goundry, "The New Reproductive Technology," 61.
- 97. As quoted by N. Barwin in testimony before the Royal Commission on New Reproductive Technologies, Ottawa, 19 September 1990, 37. The expression was originally used by B.E. Menning in *Infertility: A Guide for the Childless Couple.* Barwin added that "the hope they seek is as urgent as any immediate medical practice."
- 98. L.R. Kass, "Babies by Means of In-Vitro Fertilization: Unethical Experiments on the Unborn?" *New England Journal of Medicine* 285 (1971), 1174-79.
- 99. These comments about infertility drugs were voiced by Varda Burstyn of the National Action Committee on the Status of Women and an unnamed caller on "Radio Noon," 30 October 1990.
- 100. This idea is a paraphrasing of a statement made by British sociologist and industry observer Jalna Hanmer in a talk given to the staff of the Royal Commission on New Reproductive Technologies, Ottawa, 17 July 1991.
- 101. M.W. Lord, "A Plea for Corporate Conscience," *Harper's Magazine* 268 (June 1984), 13-14.
- 102. Pharmaceutical Manufacturers Association of Canada, "The Canadian Pharmaceutical Industry: A Backgrounder" (Ottawa: PMAC, 1991), 1.
- 103. G. Breton, Une appréciation de la position stratégique des entreprises pharmaceutiques québécoises (Montreal: École des hautes études commerciales, Centre d'études en administration internationale, 1990), 41.
- 104. Canada, Patented Medicine Prices Review Board, *Third Annual Report (for the year ended December 31, 1990)* (Ottawa: Minister of Supply and Services Canada, 1991), 5.
- 105. J. Sawatsky and H. Cashore, "Inside Dope: The Multi-Million Dollar Sellout of Canada's Generic Drug Industry," *This Magazine* (August-September 1986), 5.
- 106. Ibid.
- 107. Canada, Commission of Inquiry on the Pharmaceutical Industry, *Report* (Ottawa: Minister of Supply and Services Canada, 1985), xvii.
- 108. Sawatsky and Cashore, "Inside Dope," 9.
- 109. Patented Medicine Prices Review Board, Third Annual Report, 3.

- 110. A. Walmsley, "Pill Hill North: Canadians Have Joined the Global Race to Perfect the Latest Generation of Wonder Drugs," *Report on Business* 8 (October 1991), 46.
- 111. J. Lexchin, The Real Pushers: A Critical Analysis of the Canadian Drug Industry (Vancouver: New Star Books, 1984), 87.
- 112. Applied research consists of testing potential drugs on animals and humans.
- 113. Product development includes areas such as developing new dosage forms or different forms of existing drugs.
- 114. Lexchin, Real Pushers, 101. More recent information from PMAC indicates that this figure may be higher than 8 percent.
- 115. Statistical data courtesy of IMS Canada, Dorval, Quebec.
- 116. "The Top 1000 Companies," Report on Business (July 1991).
- 117. PMAC, "The Canadian Pharmaceutical Industry," 2.
- 118. Walmsley, "Pill Hill North," 39.
- 119. The representative interviewed was Samuel Isaly.
- 120. Walmsley, "Pill Hill North," 39.
- 121. Ibid., 43.
- 122. V. Ross, "Between Bliss and Bedlam," *Maclean's* (8 December 1980), 40; cited in J. Lexchin, "Doctors and Detailers: Therapeutic Education or Pharmaceutical Promotion?" *International Journal of Health Services* 19 (1989), 666.
- 123. J. Graedon, "Women and Drug Advertising," *Medical Self-Care* (Summer 1983), 17.
- 124. Cited in E. Hemminki, "Review of Literature on the Factors Affecting Drug Prescribing," Social Science and Medicine 9 (1975), 112.
- 125. Ibid.
- 126. Lexchin, "Doctors and Detailers," 671.
- 127. R. Mickleburgh, "Canadian MDs Agree to Stringent Code on Gifts," *Globe and Mail* (14 August 1991), A1, A2.
- 128. This statistic was cited by Jalna Hanmer in a talk given to Commission staff on 17 July 1991.
- 129. Canadian legislation does not prohibit physicians from using a drug for an unapproved use. It does, however, prohibit a pharmaceutical company from advertising a drug for an unapproved use. It is the job of the Pharmaceutical Advertising Advisory Board (PAAB) to screen out any such infractions. A call to the Deputy Commissioner of the PAAB in relation to this ad revealed that, technically speaking, the advertising of these drugs in this publication is not against the law, but the decision on the part of the manufacturers to advertise these drugs in a journal of obstetrics and gynaecology does raise some serious ethical questions relating to the indirect promotion of the use of a drug for an indication that has not yet been approved. (The manufacturers in question are Hoechst [Suprefact®], ICI Pharmaceuticals [Zoladex®], and Abbott Pharmaceuticals [Lupron®].)
- 130. J.W. Hawkins and C.S. Aber, "The Content of Advertisements in Medical Journals: Distorting the Image of Women," Women and Health 14 (2)(1988), 45.

- 131. Another example of a product that has not been approved for use in IVF but that is currently being used for that purpose is a gonadotropin-releasing hormone (Gn-RH) agonist manufactured by Syntex. It is used primarily for treatment of endometriosis.
- 132. Lexchin, "Doctors and Detailers," 664.
- 133. D. Woods, "PMAC to Spend \$1 Million Annually to Reach 'Stakeholders'," Canadian Medical Association Journal 134 (1986), 1389.
- 134. A staff person in the Customer Service Department of the CPA in Ottawa indicated that physicians are asked to make a contribution to the CPA, if they choose, in exchange for the free copy.
- 135. R.W. Bell and J.W. Osterman, "The Compendium of Pharmaceuticals and Specialties: A Critical Analysis," *International Journal of Health Services* 13 (1983), 111.
- 136. Ibid., 114, 116. Until recently, the *CPS* was distributed free of charge not only to physicians, but to pharmacists, nurses, hospitals, and recent graduates in medicine and nursing.
- 137. Lexchin, Real Pushers, 144.
- 138. Ontario Medical Association, Continuing Medical Education Programs for Ontario Physicians, 91-92 Directory (Toronto: OMA, 1991), 49.
- 139. "Overcoming Ovulation Obstacles" and "Therapy for Ovulation Disorders," Serono Symposia, USA.
- 140. Ovarian hyperstimulation syndrome occurs when the ovaries have been stimulated to over-produce follicles. The result can be painful and can lead to rupture and internal bleeding.
- 141. Z. Shoham, A. Zosmer, and V. Insler, "Early Miscarriage and Fetal Malformations After Induction of Ovulation (by Clomiphene Citrate and/or Human Menotropins), In Vitro Fertilization and Gamete Intrafallopian Transfer," Fertility and Sterility 55 (1991), 9.
- 142. Hemminki, "Review of Literature," 112.
- 143. Québec, Conseil des affaires sociales et de la famille, *Médicaments ou potions magiques?* ([Sillery]: Conseil des affaires sociales et de la famille, 1982), 56.
- 144. J. Groeneveld and M. Shain, *The Domestic Violence Survey: A Preliminary Report* (Toronto: Addiction Research Foundation, 1989), 15. Many women were also carrying prescriptions for other types of mood-modifying drugs; a full 70.4 percent of the women surveyed in the shelters had taken some type of licit drug at least once in the previous 12 months.
- 145. Canadian Medical Association, "Physicians and the Pharmaceutical Industry: CMA Policy Summary," Canadian Medical Association Journal 146 (1992), 388A-388C.
- 146. The Department of National Health and Welfare is also sensitive to the industry's image. In a document produced by the Drugs Directorate in 1990 relating to a proposed program for drug product licensing, it noted that "the ideal system should enhance the public image of the stakeholders by creating an atmosphere of openness and co-operation where information is shared and timely action is taken

on the safety and efficacy of marketed drug products," and that a continual assessment of drugs would "enhance the confidence of the public in the safety and efficacy of drugs" (Canada, Health and Welfare Canada, Drugs Directorate, "Drug Product Licensing," Ottawa: Health and Welfare Canada, 1990), 9.

- 147. Woods, "PMAC to Spend," 1389.
- 148. Ibid.
- 149. Source unknown.
- 150. Canada, Statistics Canada, *The Health of Canadians: A Report of the Canada Health Survey*, Cat. 82-538 (Ottawa: Minister of Supply and Services Canada, 1981), 180. It is worth noting that, in an analysis of drug consumption patterns of women and men for the Canada Health Survey, the data gatherers did not include birth control pills, hormone replacement therapy, or other hormonal preparations for women. Even excluding this category of drugs, which is almost exclusive to women, women still came out as greater consumers of prescription medication.
- 151. K. McDonnell, ed., *Adverse Effects: Women and the Pharmaceutical Industry* (Toronto: Women's Press, 1986), 3.
- 152. Cited in A.E. Courtney and T.W. Whipple, Sex Stereotyping in Advertising (Lexington: Lexington Books, 1983), 6-7.
- 153. J. Prather and L.S. Fidell, "Sex Differences in the Content and Styles of Medical Advertisements," *Social Science and Medicine* 9 (1975), 23-26; E.H. Mosher, "Portrayal of Women in Drug Advertising: A Medical Betrayal," *Journal of Drug Issues* 6 (1976), 72-78; R. Seidenberg, "Images of Health, Illness, and Women in Drug Advertising," *Journal of Drug Issues* 4 (1974), 264-67.
- 154. A.R. Ford, "Hormones: Getting Out of Hand," in *Adverse Effects: Women and the Pharmaceutical Industry*, ed. K. McDonnell (Toronto: Women's Press, 1986); S. Tudiver, "Becoming Healthy Skeptics: Women and Pharmaceuticals" (Winnipeg: Manitoba Council for International Co-operation, 1990).
- 155. L. Guyon, R. Simard, and L. Nadeau, Va te faire soigner, t'es malade (Montreal: Stanké, 1981), cited in Québec, Conseil des affaires sociales, Médicaments, 55.
- 156. Hawkins and Aber, "The Content of Advertisements," 43-59.
- 157. Courtney and Whipple, Sex Stereotyping, 5.
- 158. Prather and Fidell, "Sex Differences of Medical Advertisements," 26.
- 159. Tudiver, "Becoming Healthy Skeptics," 10.
- 160. Notes from a presentation by Wendy Williams, member from Newfoundland to the PMAC Advisory Panel on Women and the Pharmaceutical Industry, to the PMAC 76th Annual General Meeting, Toronto, 26 October 1990.
- 161. These drugs are not used exclusively by women; certain endocrine disorders and cancer of the reproductive organs in men are sometimes treated with hormonal preparations. For example, DES remains on the market today because of its use in prostate cancer in men.
- 162. Breton, Une appréciation, 196-97. Data supplied to Breton by IMS Canada.
- 163. S.S. Epstein, *The Politics of Cancer* (San Francisco: Sierra Club Books, 1978), 224.

- 164. Ibid., 237.
- 165. D. Lipovenko, "The Thalidomide Kids Have Grown Up," *Globe and Matl* (13 June 1987), D1, D4. Admittedly, not all thalidomide victims have received sympathetic treatment. Some were treated as freaks, believed to be children of the devil. And because of their visible disability, they have also been the victims of insensitive, gawking bystanders hurling insulting comments.
- 166. E.R. Greenberg et al., "Breast Cancer in Mothers Given Diethylstilbestrol in Pregnancy," New England Journal of Medicine 311 (1984), 1393-98.
- 167. Dutch health activists Anita Direcks and Ellen 't Hoen note that they found evidence of the continued use of DES in pregnancy in different countries at the 1985 World Conference of the UN Decade for Women held in Nairobi. They met a Kenyan doctor who listed several brand names of DES still being prescribed to pregnant women at her hospital and heard reports from representatives from Brazil, Costa Rica, Rwanda, Peru, and Zaire about the continued use of DES in pregnancy in their countries. A. Direcks and E. 't Hoen, "DES: The Crime Continues," in Adverse Effects: Women and the Pharmaceutical Industry, ed. K. McDonnell (Toronto: Women's Press, 1986), 44-49.
- 168. M.L. Braun, "Still with Us: Research Needs of the DES-Exposed," DES Action Voice 49 (Summer 1991), 6.
- 169. The figure of 500 000 exposed individuals is considered a conservative estimate by some. It is based on both an extrapolation from American figures and the number of cases of the rare form of DES-related cancer already detected in Canada.
- 170. Braun, "Still with Us," 7.
- 171. Jarrell, Testimony before the Commission, 119-20.
- 172. Based on a telephone conversation with a product manager of a Toronto-based affiliate of a multinational pharmaceutical company, 10 September 1991.
- 173. As reported in the 1990 Annual Report of the Ares Serono Group. Serono Canada is also involved in sponsoring educational symposia and allied health programs in conjunction with the Canadian Fertility and Andrology Society, as well as assisting the IAAC in the publication of its newsletter.
- 174. A written submission from Organon Canada Ltd. to the Royal Commission on New Reproductive Technologies, April 1991, 13.
- 175. Ares Serono Group Annual Report, 1990. Data provided by IMS Canada.
- 176. Data provided by IMS Canada.

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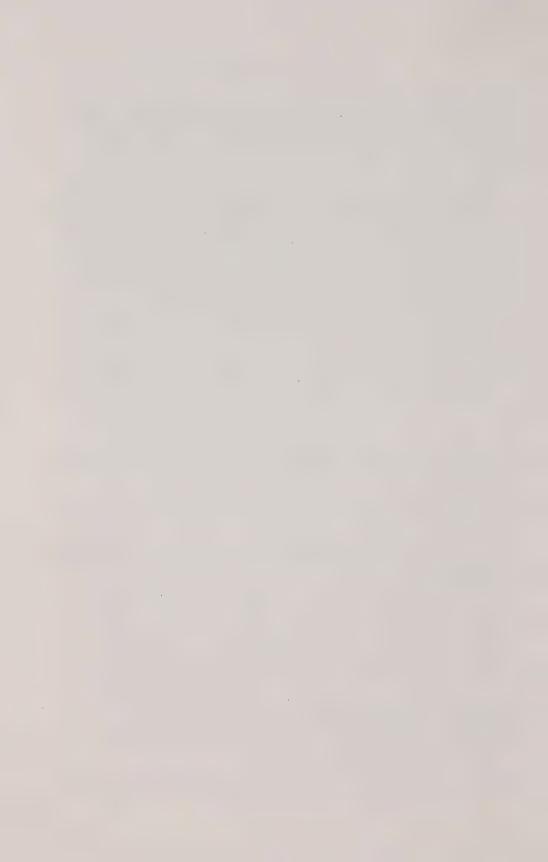
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Commercial Involvement in New Reproductive Technologies: An Overview

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Executive Summary

The purpose of this document is to study the role of commercial interests in the provision and development of new reproductive technologies (NRTs). The author examines the role played by the pharmaceutical, biotechnology, and medical devices industries in providing products and services used for NRTs. She focuses particularly on the use and development of genetic techniques within these three industries, as well as in commercial genetic testing.

This analysis deals with most of the technologies covered by the mandate of the Royal Commission on New Reproductive Technologies. The author discusses the commercial potential of NRTs, firms active in this area, the size of markets, and the forces governing these industries.

The Canadian pharmaceutical industry includes 148 firms that manufacture and distribute pharmaceutical products in Canada. Most are subsidiaries of multinational companies. The Canadian market totals about \$4.2 billion. The author examines in detail governmental controls on the industry, particularly in relation to research and drug

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trials. There are over 18 000 medications for sale in Canada. About 3 000 of them are found in the *Compendium of Pharmaceuticals and Specialites*. Only eight products in the compendium are classified as fertility drugs. Five others are classified as drugs used to treat endometriosis. The Canadian market for fertility drugs is estimated at \$16 million (four-tenths of 1 percent of the total Canadian pharmaceutical market). Seventy-five percent of the market is held by a single firm. The author surveyed 70 pharmaceutical companies on their perception of the market for fertility drugs. The vast majority considers this market too small to be of interest.

The Canadian biotechnology industry includes between 300 and 400 firms, which work in a variety of areas. About 94 companies are working in the areas of health care, therapeutic agents, and diagnostics. Despite the widespread opinion that these firms comprise one of the main driving forces in the development of genetic technologies with potential application to NRTs, this does not seem to be the case in Canada. In fact, Canadian research in genetic techniques is conducted primarily in universities and genetics centres, and the industry's activities are extremely limited in this regard.

The author studied the commercial potential of genetic techniques, especially those associated with screening for hereditary diseases or used for prenatal diagnosis. Although universities and research institutes subsidized by governments and charities conduct considerable research in this area, little is done by the private sector in Canada. Pharmaceutical companies in particular are not involved in this field. On the whole, the most substantial profits in the area of genetic techniques will probably be made by firms that perfect simple, accurate screening tests for common hereditary diseases.

The Canadian medical devices industry includes about 650 firms that market 6 500 categories of products, from gauze bandages to medical computer systems and needles used to aspirate oocytes for in vitro fertilization. The Canadian market totals about \$2.5 billion, and 85 percent of the products are imported, especially from the United States. The market for devices used in assisted reproduction is considered minute, whereas the market for laboratory products (reagents) used in conjunction with IVF and assisted reproduction is more substantial: about \$7 million. Commercial laboratory testing related to fertility and assisted reproduction is estimated at \$14 million.

Introduction

The purpose of this paper is to explore the role commercial interests play in providing and furthering new reproductive technologies (NRTs). Specifically, the role of the pharmaceutical, biotechnology, and medical devices industries in providing products and services used in NRTs will be examined. Most, but not all, of the technologies that fall within the mandate of the Royal Commission on New Reproductive Technologies are

included; commercial involvement in embryo and fetal tissue research is not covered.

A wide range of business and corporate interests are now involved in NRTs — from the manufacture and sale of fertility drugs and test materials (reagents) used to measure hormone levels to the sale of sophisticated automated computer systems used to study human chromosomes, and specialized catheters and needles employed in egg retrieval and embryo transfer. The potential for further commercial involvement in many of these technologies is significant. The genetic technologies in particular (carrier identification, prenatal diagnosis, preimplantation diagnosis, and gene therapy) are thought to hold "huge" commercial potential for companies developing tests and techniques that lend themselves to mass screening or wide therapeutic use outside research settings. This paper looks at the commercial potential of NRTs, the companies involved, the sizes of markets, and the forces driving these industries.

The information contained in this paper was gathered from a variety of sources, including documents published by professional organizations, industry associations, and government agencies such as Industry, Science and Technology Canada (ISTC), the Science Council of Canada, the Patented Medicine Prices Review Board (PMPRB), the Drugs Directorate of Health and Welfare Canada, the Industrial Biotechnology Association of Canada, the Pharmaceutical Manufacturers Association of Canada (PMAC), the Canadian Drug Manufacturers Association (CDMA), the Canadian Pharmaceutical Association (CPA), and Medical Devices Canada (MEDEC). In addition to these organizations, more than 75 individuals in Canada and the United States provided valuable information and insight. Some of these people are involved in the pharmaceutical, biotechnology, and medical devices industries. Others are business analysts, scientists, academics, or corporate representatives.

The contributions of individuals directly involved in the various industries were particularly important because little published information exists on markets or sales volumes for specific products and services. In most cases, data on products used for NRT applications are reported only in combination with much broader market information.

In addition, a survey was conducted of PMAC member companies to elicit information about their involvement in producing and developing products used in NRTs. A sample survey questionnaire is found in Appendix 2; results of the survey are included in Appendix 3.

The paper is divided into four sections: the pharmaceutical industry, the biotechnology industry, genetic technologies, and the medical devices industry. It is important to recognize, however, that considerable overlap exists among these industries, which together supply the health care market in Canada. There is significant overlap, for instance, between the pharmaceutical and medical devices industries. Many large pharmaceutical companies have diagnostics divisions that produce items (including reagents and computerized systems) used in laboratory testing; some count

medical and surgical supply companies among their affiliates or corporate

groups.

The distinction between the pharmaceutical and biotechnology industries is even more problematic, in that many traditional pharmaceutical companies use biotechnology — molecular biology and recombinant deoxyribonucleic acid (DNA) techniques — to some extent in manufacturing their products. In a very real sense, biotechnology is not an industry at all, but a technology used in diverse industrial sectors from mining and forestry to aquaculture.

Those companies that specialize in using biotechnology to make health products (diagnostic and therapeutic) are sometimes collectively referred to as the *biotechnology industry*. A number of these companies are divisions of major pharmaceutical firms. Others are small boutique operations. Canada's largest biotechnology company, Allelix Biopharmaceuticals, is, as its name implies, a hybrid; it claims a place within the Canadian

pharmaceutical industry through its membership in the PMAC.

Exactly where genetic technologies fit in is even less clear. In fact, commercial activity in genetic technologies is found in the three industries already mentioned — pharmaceutical, biotechnology, and medical devices — and involves a fourth, the commercial laboratory testing industry (discussed in Section 4, with medical devices).

Major pharmaceutical companies are engaged in a great deal of research directed toward discovering the genetic or molecular basis of hereditary disease, particularly of multifactor conditions such as cancer and heart disease. Their hope is that a better understanding of the genetic basis of these diseases will lead to development of effective drugs to treat them. A subsector of the biotechnology industry includes companies engaged primarily in developing tests and screening techniques for hereditary disease. Most companies involved in this field commercially are located in the United States. Corporations in the medical devices industry are also beginning to take an interest in the field of genetic testing — by developing automated systems for mass screening, for instance.

Very little *commercial* activity in the genetic testing and screening field is carried out in Canada; indeed, most information sources are academics and researchers. Although a separate section of this paper is devoted to a discussion of the commercialization of these technologies, they are not generally thought of as a separate industry — at least not yet and not in Canada.

In summary, the industries discussed in this paper are not distinct and exclusive entities. There is a great deal of overlap and ambiguity. Efforts to definitively fit certain commercial activities into one category or another may be more of a hindrance than an aid to understanding.

Section 1. The Pharmaceutical Industry

Overview

Approximately 148 companies manufacture and market pharmaceutical products in Canada. These companies fall into two main groups: the research-based (brand-name) manufacturers, largely represented by the Pharmaceutical Manufacturers Association of Canada (PMAC) with 67 members, and the generic manufacturers, represented by the Canadian Drug Manufacturers Association (CDMA) with 19 members.

The majority of these companies are subsidiaries of multinational corporations. In 1990, the leading 30 companies supplied roughly 80 percent of total drug purchases by hospitals and drugstores.² Only two of these companies are Canadian-owned; both are producers of generic medicines, and together they account for the majority of generic sales in

Canada.3

Only 18 percent of PMAC member companies are Canadian-owned, while 51 percent are U.S.-based and 31 percent are Western European.⁴ The Canadian pharmaceutical industry is centred in Ontario (51 percent) and Quebec (32 percent); Western Canada is home to 15 percent of companies, and the Atlantic provinces, 2 percent.⁵

Products manufactured by pharmaceutical companies include medicines, agricultural and veterinary products, fine chemicals, and toiletries. Almost half (47 percent) of the products are non-prescription items, while 45 percent are sold by prescription. Veterinary and biological

products account for 8 percent of the total.6

The size of the Canadian market for pharmaceuticals is approximately \$4.2 billion. In 1989, generic products were used to fill more than one-quarter of all prescriptions; however, revenues from these sales represented less than 10 percent of the total pharmaceutical market, according to Wayne Schnarr, research director of the CDMA. On average, generic drugs cost 30 to 40 percent less than brand-name products and save Canadians \$300 million annually.

The active ingredients (fine chemicals) for most pharmaceutical products manufactured in Canada (generic and brand-name) are imported from other countries. By and large, Canadian manufacturing activity involves compounding the finished product as well as packaging and labelling final dosage forms. Importing finished products to supply the

Canadian market is less common.

Historically, a major difference between brand-name and generic companies has been the former's commitment to research and development (R&D). In recent years, however, generic companies have increased R&D spending and now devote approximately 10 percent of their annual sales to it in this country.⁹

Development costs associated with bringing a new pharmaceutical product to market are high and can only begin to be recouped after a drug has been approved by the Health Protection Branch (HPB), Health and Welfare Canada, with the issuance of a Notice of Compliance. Some new drugs find a solid market niche and show steady sales for many years. Others are developed and successfully marketed only to be supplanted by new and better agents within a few years.

Frequently quoted industry statistics suggest that only 1 of every 10 000 compounds originally synthesized and studied for their pharmacological properties makes it to market. The average development price tag, including costs of failed attempts, is some \$250 million for each drug that reaches the market. The average time between the discovery of a compound and government approval to market the drug is 10 to 12 years.

Patent Protection and Licensing

In 1987, amendments were made to the Canada Patent Act with Bill C-22. 11 Patents on drugs now cover a period of either 17 or 20 years, depending on the filing date. If the application was submitted prior to 1987 (no matter when approved), the patent is granted for 17 years from the date the patent is *issued*. For applications submitted from 1987 to 1989, pre-1987 rules apply, with minor variations.

On 1 October 1989, the clock started ticking on future patent lives of a maximum of 20 years from the time a patent application was *submitted*. ¹² In other words, under current rules the clock starts running down on potential patent life as soon as the application is submitted, even though up to five years may elapse between the time of application and the issuing of the patent. Several more years of patent life may be consumed during clinical trials, which may or may not be concurrent with the patent waiting period, and another three years will pass, on average, awaiting HPB approval to market the drug. The net result is that up to half the patent life may have expired by the time the product reaches the market.

Not all prescription drugs are patented. In some cases, patents have expired or have been dedicated to the public domain by the originator of the drug. In addition, certain pharmaceutical products — notably, known naturally occurring hormones — cannot be patented. Most of the major fertility drugs, for instance, are non-patented, either because patents have expired or the drugs are naturally occurring hormones.

For patented drugs, the company holding the patent does not necessarily retain exclusive rights to market that drug for the duration of the patent. Under a system of compulsory licensing introduced in 1969, generic manufacturers may apply for permission to produce and market equivalent copies of patented drugs once the innovating company's period of market exclusivity runs out. "The Commissioner of Patents [Consumer and Corporate Affairs Canada] decides whether a compulsory licence will be granted and establishes a royalty rate to be paid to the patent holder." "13

Since 1987, the period of market exclusivity (patent protection) granted to the innovating company has been set at seven or ten years (ten years if a drug's active ingredient is made in Canada). The manufacturer receives market exclusivity for seven or ten years, or for the remaining life of the patent, whichever is less.¹⁴

In January 1992, the federal government, in the midst of General Agreement on Tariffs and Trade (GATT) negotiations, announced that it intends to do away with compulsory licensing of pharmaceuticals, thereby restoring full patent protection for the life of the patent. This move has provoked strong protest on the part of the Canadian generic pharmaceutical industry, which says the change will destroy it.

Research and Development

In exchange for the period of patent protection provided by Bill C-22, PMAC member companies made a commitment to increase R&D investment in Canada to 10 percent of sales by 1996. By 1990, PMAC companies had increased R&D levels to 9.2 percent of sales (\$281 million)¹⁵ and reported reaching 10 percent during 1991. PMAC spending on basic research was \$70.1 million in 1990, 26.3 percent of the total R&D, up 30.9 percent from 1989.

Table 1. Total R&D Expenditures* and R&D to Sales Ratios, 1990, 1989 and 1988

		Total R&D expen- ditures (\$M)	% Change from previous year	sales	% Change from previous year	R&D to sales ratio	
Year	Companies reporting (N)					All	PMAC patentees (%)
1990	63	281.3	14.9	3 203.6	7.7	8.8	9.2
1989	66	244.8	47.7	2 973.0	9.4	8.2	8.1
1988	66	165.7		2 718.0		6.1	6.5

^{*} Total expenditures include capital equipment expenditures and allowable depreciation expenses.

Source: Patented Medicine Prices Review Board, *Third Annual Report* (Ottawa: Minister of Supply and Services Canada, 1991), 19.

At issue is the kind of research that qualifies in determining the R&D-to-sales ratio. Only those R&D expenditures eligible for the Revenue Canada scientific research and experimental development tax credit are included in calculating the ratio. 18 The rules are quite stringent in

determining what kind of research qualifies — so stringent, in fact, that the PMAC claims the rules may limit the ability of companies to fund basic research. 19

Drug Pricing

In 1987, the PMPRB (Patented Medicine Prices Review Board) was created under amendments (Bill C-22) to the Patent Act to "protect consumer interests" and ensure that drug prices do not rise excessively as a result of the new patent protection.²⁰ The PMPRB is an independent quasi-judicial body with a threefold mandate:

- 1. to ensure that the prices of patented medicines charged by patentees are not excessive;
- 2. to report annually on pricing trends in the pharmaceutical industry; and
- 3. to report annually on the ratios of R&D expenditures to sales for individual patentees and for the patented pharmaceutical industry as a whole (the board has no power to direct the level or nature of R&D expenditures of pharmaceutical companies).²¹

The PMPRB reviews the prices of all patented medicines sold in Canada (43 percent of total sales at the factory gate)²² but has no regulatory authority over non-patented products. Under Section 39 of the Patent Act, the Board, after holding a formal hearing to review the matter, has the power to order that the price of a patented medicine be reduced. To date, according to the Board, voluntary compliance has worked well. Though discussions on pricing have taken place with some manufacturers and "understandings" have been reached, it has not been necessary to hold formal hearings or to order price reductions.

The PMPRB reviews only the prices charged by manufacturers to wholesalers, hospitals, and pharmacies; its jurisdiction does not extend to the prices charged at the retail level. 23

From 1983 to 1987, the pharmaceutical component of the Industrial Products Price Index increased at an average annual rate of 7.1 percent. The Consumer Price Index (CPI) rose 4.3 percent per year for the same period. Since 1987, when Bill C-22 came into effect, drug prices increased 5.1 percent per year, compared to the CPI annual increase of 4.7 percent. However, the prices of patented products within the PMPRB's jurisdiction increased at an average annual rate of 3.1 percent, below the rate of inflation.²⁴

The pharmaceutical industry remains a top performer within the Canadian economy in terms of profitability, in spite of price levelling and increased R&D spending. It is also considered to be relatively resistant to recession. According to Industry, Science and Technology Canada (ISTC) data, the average rate of growth of the gross domestic product for the industry was 4.4 percent (in constant 1981 dollars) over the five years

ending in $1989.^{25}$ "After-tax profits on total income for the pharmaceuticals industry averaged 8.3 percent annually from 1979 to 1987 ... compared with 3.7 percent annually for all manufacturing."

Regulation

Before a drug can be marketed in Canada, it must receive a Notice of Compliance from the HPB (Health Protection Branch) of Health and Welfare Canada.

Several stages of drug testing are required (Table 2), and extensive data on the findings of tests and clinical trials are reviewed by the HPB at each stage in the process before approval is given to proceed to the next.

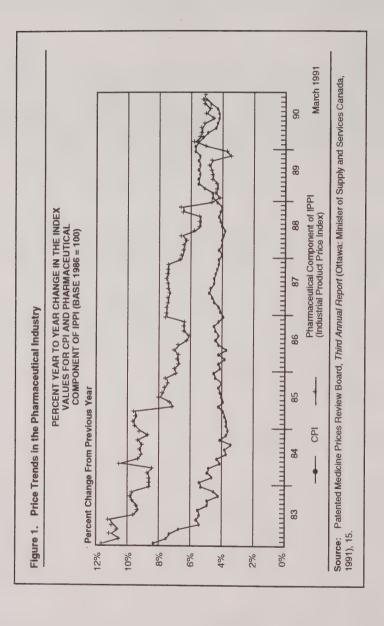


Table 2. Stages in the Development and Approval of a New Drug in Canada

Research Regulation Discovery of new drug: chemical synthesis or extraction, analysis, formulation. Preclinical New Drug Submission (PNDS): available information on new drug. Review by Health Protection Branch (HPB) of Health and Welfare If approved, company may proceed to Canada. clinical testing. Protocols: detailed descriptions of proposed clinical tests on humans; each is reviewed and approved by HPB and is subject to ethical review of research institution and informed consent of subjects. Phase 1 protocol: toxicology, small sample of healthy subjects. Phase 1 clinical research Phase 2 protocol: therapeutic effect, toxicology, small sample of patients. Phase 2 clinical research Phase 3 protocol: therapeutic effect, toxicology, large sample. Phase 3 clinical research New Drug Submission (NDS): complete information on new drug including full report on clinical tests. If approved receives Notice of Compliance (NDS/NOC) and Product Monograph. Marketing Phase 4 clinical research: no approval is required.

Note: Research reported for PNDS and NDS need not be done in Canada.

Source: Canada, Commission of Inquiry on the Pharmaceutical Industry, Report (Ottawa: Minister of Supply and Services Canada, 1985), 373.

When applying to the HPB for approval to market a new drug in Canada, the manufacturer must file a New Drug Submission (NDS), a collection of data that has been described as "an exhaustive set of documents, often of several hundred volumes." A NDS includes details of all experiments conducted on the drug in Canada and in foreign countries.

Data from clinical trials conducted outside Canada may be accepted in support of a NDS if they are judged by the HPB to be of adequate quality. Foreign data are subjected to detailed scientific evaluation before they are accepted. There is no formal requirement that Canadian data be included; that decision is made on a case-by-case basis. In addition to the scientific rigour of out-of-country data, the HPB examines whether test subjects in foreign trials are representative of the intended patient population in Canada in terms of age, sex, race, overall general health, and other factors.²⁸

From January 1981 to July 1984, 11 of 66 NDSs that received approval (17 percent) included no Canadian study data. ²⁹ More recent figures are not available, but according to Dorothy Walker, Acting Head of the Bureau of Human Prescription Drugs, the majority of submissions entering the HPB's review process over the past five years include some Canadian data. In most cases, however, Canadian data account for a small proportion of the total data submitted.

Certain drugs known as "biologics" (listed in Schedule D to the Food and Drugs Act) are subject to especially rigorous controls. This category includes blood derivatives, certain hormones and enzymes extracted from animal or human tissues or from cultures of micro-organisms, and drugs produced by modern biotechnology (genetic engineering).

The manufacture of these drugs is complex, and exacting quality control tests must be conducted on each lot prior to its release. Several of the major hormonal drugs used to treat infertility are Schedule D drugs.

Since manufacturing of these products is intricate and critical to the final product, the premises in which they are manufactured must be inspected and licensed by the Bureau of Biologics before they can be sold in Canada. The bureau has its own laboratories and routinely tests virtually every lot of every licensed product before permitting them to be distributed for sale. The regulatory requirements for drugs listed in Schedule D exceed those for other products and constitute the most rigorous of controls on safety and effectiveness of all drugs in Canada. ³⁰

Currently, the HPB review process for NDSs takes about three years, but the backlog of 1 500 submissions that existed five years ago has been significantly reduced. At the end of 1991, 225 NDSs and 156 Supplemental NDSs were under review within the Bureau of Human Prescription Drugs; of those, 127 and 59, respectively, were backlogged (under review for more than 180 days). For the Bureau of Biologics, the numbers were 42 NDSs and 53 Supplemental NDSs (required for any changes to a product

monograph, i.e., new product format, dosing schedule changes, or new treatment indications); of those, 19 and 23, respectively, were backlogged.³¹

Despite improvements, the industry perceives the review process as being very slow. To help alleviate this bottleneck (here and in other countries), there is a move afoot internationally to develop a central drug registry system with clinical trials based on international protocols. The aim would be to eliminate the need for separate clinical trials in each country, thereby speeding approvals and reducing drug development costs. Most likely, clinical trials would be conducted in a "basket" of countries that best represent the population profiles of expected users of the drug. Preclinical R&D and post-marketing surveillance would continue in each country.

Reporting of Adverse Reactions

At the present time in Canada, pharmaceutical manufacturers are responsible for reporting to the HPB all adverse drug reactions that come to their attention by submitting an Adverse Reaction Report. This obligation applies only to new drugs (generally those on the market seven years or less). The system relies on physicians to report adverse reactions or their suspicions of such reactions to the manufacturer concerned. Reporting by physicians is entirely voluntary, however, and may result in only a small percentage of such incidents being reported to the HPB. There is no requirement for either physicians or manufacturers to report adverse reactions of older drugs; any reporting is now done on a voluntary basis, although this situation is in the process of being changed.

The HPB now receives between 5 000 and 6 000 Adverse Reaction Reports per year. Its Product-Related Diseases Division is currently developing a new post-marketing surveillance program intended to increase the evaluation and follow-up components of its work. In the past, the HPB's emphasis has been on evaluating drugs prior to marketing. The intention under the new program will be to shift some of that emphasis to the post-marketing period, according to Curt Appel, acting chief of the Product-Related Diseases Division.

Non-Approved Indications

When a Notice of Compliance is issued allowing a drug to be sold in Canada, it is approved only for use in treating certain disease states. These specified disease states are known as "approved indications." By law, drug companies can promote their products for approved indications only, but once a drug is on the market, physicians are free to prescribe it for whatever purposes they wish, based on their own clinical judgment. This means that, not infrequently, drugs are prescribed for purposes other than their approved indications.

There are a number of reasons a physician might issue such prescriptions. Frequently, drugs are approved for other indications outside

Canada. Physicians become aware of alternative uses for drugs through medical literature, foreign colleagues, and international conferences. Many physicians have received part of their training abroad. In addition, an approved drug may be undergoing clinical trials in Canada or elsewhere to study potential new indications. Results of such trials are often published long before the HPB approves the new indication.

The drug leuprolide acetate (Lupron®, manufactured by TAP Pharmaceuticals of North Chicago and distributed by Abbott Laboratories in Canada) is a case in point. This drug is approved in Canada only for the treatment of prostate cancer. In the United States, it has also been approved since October 1990 for the treatment of endometriosis (a gynaecological condition that may interfere with fertility), and, according to Adele Bourgeault of Abbott Laboratories, it is under review for this indication in Canada. It is also sometimes used in conjunction with *in vitro* fertilization (IVF) to suppress the normal hormonal cycle before an IVF treatment cycle is started.

Canadian sales of this drug increased 50 percent in the period from September 1990 to August 1991.³² According to industry sources, a significant portion of this increase was due to use of the drug for endometriosis.

To understand why Lupron® might be useful in these areas requires some knowledge of reproductive endocrinology. Basically, the drug suppresses production of luteinizing hormone (LH), which stimulates testosterone production in the male and estrogen production in the female. Theoretically, therefore, it might be useful in treating any condition where the desired effect is to suppress testosterone in the male or estrogen in the female.

Another example of a drug used for non-approved indications posed a dilemma for transplant surgeons. Ortho Pharmaceuticals produces a drug originally approved to prevent organ rejection in kidney transplant patients. But while the company waited for HPB approval for two new indications (heart and liver transplantation), surgeons began using it for these non-approved indications, believing the potential benefit outweighed concerns about unsanctioned use.

According to Paul O'Brien of the HPB's Drug Regulatory Affairs Division, the HPB has little or no control over how a drug is used once it has been approved. If there is concern over the safety of a drug, the HPB has the power to withdraw the Notice of Compliance, or it may write a letter to all Canadian physicians informing them of the problem (see sample letters, Appendix 1). Generally, this occurs once or twice a year (four have been issued since 1988). Only once in recent memory has a HPB information letter dealt with a drug's indications. That letter dealt with Genentech's recombinant growth hormone, Protropin[®], which had been granted approval for a particular indication provided the company furnished certain data. Subsequently, the company indicated it was not

able to conduct the long-term studies required, and the indication was withdrawn at the company's request.

Responsibility for maintaining standards of medical practice and disciplining physicians rests with the College of Physicians and Surgeons in each province. However, disciplinary action for inappropriate drug prescribing usually centres on over-prescribing of narcotic drugs or other controlled drugs, for example, anabolic steroids. According to the College of Physicians and Surgeons of Ontario, it is common for drugs to be used for purposes other than approved indications. Frequently, manufacturers do not seek approval for minor indications because they do not sell enough of a drug for that particular purpose to justify the expense involved in gaining approval. Dr. John Carlisle, deputy registrar of the College of Physicians and Surgeons of Ontario, believes that if drugs could be used only for approved indications, a significant number of advanced drugs used for rare conditions would not be available in Canada.

Trends in the Pharmaceutical Industry

Biotechnology

Increasingly, major therapeutic advances in human health products are based on molecular biology research and DNA technology. Pharmaceutical products developed using these technologies tend to be highly specialized, "tailored" drugs aimed at small patient populations — for example, human growth hormone and erythropoietin for kidney dialysis patients. The drug tissue plasminogen activator manufactured by Genentech under the brand name Activase® is an exception, as the potential market is large. The drug is used in acute myocardial infarction (heart attack) to dissolve blood clots quickly and thereby minimize damage to the heart.

High development costs coupled with small potential markets mean the cost of these drugs to the consumer and the health care system is high, at least initially. The companies argue that costs must be assessed using cost/benefit analysis, looking at costs to the system as a whole, not just the cost of the drug. They say that savings to the health care system arising from the availability of these drugs (not to mention improved quality of life and reduced morbidity and mortality) must also be taken into account. Factors such as reduced hospitalization, elimination of the need for surgery, and increased options for self-care must be considered, they argue.

Re-examination of Older Drugs

The industry is re-examining certain drugs that have been used for years to treat particular conditions to determine whether they offer therapeutic potential in other disease states. The rationale for this re-examination lies in a vastly improved understanding of human biology and disease processes, knowledge that sometimes points to potential new uses for older drugs.

An example is the drug methotrexate. Used for many years in cancer chemotherapy, methotrexate is now approved for the treatment of rheumatoid arthritis and is currently being studied for other indications.

This trend toward re-examining older drugs has important implications for the pricing and marketing of the resulting "new" product — implications the industry is still grappling with. Problems may arise in efforts to recoup development costs associated with gaining HPB approval to market a drug for a new indication. The process is long and costly and requires that a new series of clinical trials be conducted. Determining a market price that enables the manufacturer to fund the cost of new trials may be controversial.

In the case of methotrexate, the company's move to repackage the drug (new labelling and product information were required) and to increase the price (for arthritis use only) in order to recoup development costs proved unworkable. Consumers would not accept a higher price for one indication over another. Ultimately, a new, blended price was introduced, with the result that the cost of the drug for cancer treatment increased.

Home Health Care

A major trend in health care is the move to more community-based care, which usually means finding alternatives to costly hospitalization whenever possible. More hospital services are now being provided in clinics and outpatient settings and in day-surgery units. This trend is partly the result of spending constraints introduced by every province in reaction to rapidly escalating health care costs during the 1980s.

In hand with this trend is a move toward more home care and home support services. There is, too, an increasing awareness by many people of personal responsibility for health. According to ISTC, these trends have created a boom for the home health care market, which is expanding by 20 to 25 percent per year. Pharmaceutical companies and their subsidiaries are involved to the extent that they supply products (diagnostic kits, intravenous solutions, dialysis supplies, and certain drugs) used in the home setting.

Demographics

The aging of the population, as the baby boomers move into their middle and senior years, has important implications for the pharmaceutical industry. Drugs to treat conditions prevalent in middle age and senior years will become even more attractive to manufacturers because of their increased market potential. Drugs to treat infertility may become less attractive as the segment of the population in its reproductive years shrinks.

Consumer Awareness

Today's consumer is better educated and more inclined to question medical advice and direction than people of earlier generations were. Consumers are more apt to ask for information about drug side-effects, possible interactions, and how drugs work in the body. There is a trend toward zero tolerance of side-effects or negative outcomes resulting from medical intervention. Today's health care consumer wants to be involved in decision making and expects to exert some control over his or her health care.

Among many consumers today there is a healthy scepticism about whether drug therapy is necessarily the best answer. This attitude, coupled with a greater awareness of the importance of prevention, is placing greater demands on health care professionals to educate patients about disease prevention and healthy lifestyles, rather than automatically turning to drugs and technology. The long-term effects of drugs, particularly those used in reproductive health, are of particular concern to many consumer, advocacy, and women's groups.

Compliance

Recognizing that even the most effective drug is of no value unless the patient is willing to take it as prescribed, manufacturers are looking for better ways to encourage patients' compliance with dose schedules. If a capsule is too big to swallow easily or has to be taken four times a day, patients may skip doses, thereby reducing the effectiveness of the treatment.

New sustained-release formats, single-dose formulations, skin patches, and depot injections that release a drug gradually over time represent efforts by the industry to improve compliance. Work to develop new formulations and dosage forms constitutes a significant proportion of the R&D conducted by pharmaceutical manufacturers.

Provincial Drug Benefit Plans

Taken together, provincial drug benefit plans constitute the single largest payer for prescription drugs in the country (private drug plans are second). During the 1980s, government plans experienced a rapid escalation of costs — a phenomenon that has led to a variety of measures to contain them.

Principal among these containment measures are moves to reduce the number of drugs listed in the drug benefit formularies (the listings of drugs for which the plans will pay) and to tighten the approval process for the

acceptance of a drug into formularies.

Recently, Ontario removed from the formulary certain drugs used by people with human immunodeficiency virus (HIV) infection, a move that has outraged physicians who treat patients with acquired immunodeficiency syndrome (AIDS) and AIDS groups. Generally, it is becoming more difficult to get a drug listed; a highly convincing argument is needed to show that a new drug has significant benefits over existing drugs.

Another mechanism being used by governments to reduce drug plan costs is the requirement that pharmacists filling a prescription substitute the lowest-priced interchangeable product (often a generic drug). Such

measures vary from province to province.

Smart Card Technology

On-line systems and so-called "smart cards," which store information about an individual's prescription drug history, represent a major innovation on the horizon. Using such technology, a doctor's office or a pharmacist could gain immediate access to the entire spectrum of drugs an individual is taking, even though the patient may have several doctors and use more than one pharmacy. Using this system, doctors and pharmacists should be able to spot potentially dangerous drug interactions before they happen and make professional judgments based on complete information. In addition, such systems, if plugged into provincial drug benefit plans, would enable governments to monitor utilization patterns and would help them eliminate criminal abuses such as obtaining repeat prescriptions of narcotics from more than one doctor. Confidentiality, however, is a serious concern that will require careful evaluation.

Industry/Physician Relations

In the past, the pharmaceutical industry had drawn criticism for questionable marketing and promotional practices, such as providing doctors with expensive trips and "perks" in conjunction with educational meetings and conferences. In recent years, the industry has taken steps to improve its professionalism and integrity in its dealings with physicians and other health care providers.

The PMAC's *Code of Marketing Practices*, revised in 1988, establishes strict standards of conduct for its members to follow in dealing with health professionals. In the area of continuing education, the code specifies that the content of programs and choice of speakers for industry-sponsored symposia must be determined by independent health care organizers, not by the company itself. In addition, while grants or honoraria may be provided to health care professionals participating in a symposium, payments for travel expenses, et cetera, may not be given to spouses or family members. The code also includes a section on post-marketing studies and sets out conditions under which such studies are to be conducted.³⁴

Adherence to the code is a condition of PMAC membership; companies that flout the rules may have their memberships revoked. Complaints about a company's marketing practices are referred to the PMAC's Marketing Practices Review Committee for adjudication. A number of alleged infractions have proceeded through various steps in the adjudication process, but few have reached the final stage — an appeal panel hearing. No company has lost its membership, though a number have had to agree to cease objectionable practices.

The Food and Drug Administration (FDA) in the United States has also begun to crack down on industry promotional activities that are disguised as scientific or continuing education events. In addition, in August 1991, the Canadian Medical Association adopted a set of 38 guidelines setting out

the kinds of items doctors may or may not accept (or demand) from companies engaged in marketing products. The guidelines curtail industrysponsored gifts and activities that have nothing to do with providing health care to patients — for example, covering travel expenses to meetings and conferences in distant locations intended solely to promote a particular product.35

The Compendium of Pharmaceuticals and Specialties

"Over 18 000 drug products are offered for sale in Canada." Of these, approximately 3 000 are listed in the 1991 Compendium of Pharmaceuticals and Specialties (CPS), published annually by the Canadian Pharmaceutical Association (CPA).

The CPS is distributed to most physicians in Canada free of charge by the CPA, an organization representing professional pharmacists, not pharmaceutical manufacturers. It is the most widely used source of information about drugs in Canada but does not contain information on all 18 967 drug products listed by Health and Welfare Canada. 37

The CPS includes several different sections. The bulk of the 1991 edition consists of 1 373 "white pages," which contain alphabetical listings of drugs with a description (monograph) of each product. There are two types of monographs: general and brand-name. General monographs provide information about several equivalent (interchangeable) drugs. Brand-name monographs are either full monographs, as approved by the HPB, or abridged monographs provided by the manufacturer.

Full monographs include information about the pharmacology of the drug, its indications, contraindications, adverse reactions, and other prescribing information. In the case of drugs that were on the market prior

to 1968, full monographs may not be approved by the HPB.

Abridged monographs provide only limited information, such as the name of the drug, the manufacturer's name, and a description of the dosage forms.

According to Carmen Krogh, CPS editor-in-chief, full prescribing information is provided for approximately 80 percent of the drugs listed in

the compendium.

The pink section of the CPS contains listings of drugs by therapeutic category. Products are included in this section at the request of the manufacturer; a fee is charged for the listing, and not every drug in the white pages is listed in the pink pages. Starting with the 1992 edition, there will no longer be a pink section. Manufacturers will pay either \$750 for a full monograph in the white pages or \$300 for an abridged monograph.

Drugs Used to Treat Infertility

Of the approximately 3 000 drugs listed in the 1991 CPS, 5 drugs are categorized in the pink pages as "infertility therapy" and 2 as "ovulation stimulators": 1 drug is listed in both categories. In addition, six drugs are listed under "endometriosis therapy." The nine drugs most commonly used in the treatment of infertility are listed below. Other drugs such as antibiotics may be used in conjunction with infertility treatment, but, by and large, the drugs listed in Table 3 are the main drugs used in Canada.

Drug*	Description	
Pergonal [®] (Serono*)	A combination of LH and follicle-stimulating hormon (FSH), extracted from the urine of post-menopausa women, that acts on the ovaries to stimulate follicle (ovum development.	
Serophene [®] (Serono)	Acts on the hypothalamus to (indirectly) stimulate the release of LH and FSH.	
Profasi [®] (Serono)	A human chorionic gonadotropin (hCG) produced by the human placenta and extracted from the urine of pregnant women. Administration at mid-cycle induces ovulation.	
Metrodin [®] (Serono)	Contains FSH alone and acts on the ovaries to stimulate follicle development (used instead of Pergonal® when the LH level is already high in relation to FSH).	
Clomid [®] (Merrell- Dow)	The same as Serophene [®] (equivalent products).	
A.P.L.® (Ayerst)	Equivalent to Profasi [®] , in that it is a hCG.	
Factref [®] (Ayerst)	Similar (but not identical) in action to Pergonal [®] ; it is a synthetic product approved for use only in certain diagnostic tests to assess fertility. Dr. P. Larose of Ayerst has indicated, however, that the company believes that 90 percent of the drug's sales are connected to infertility treatment.	
Parlodel [®] (Sandoz)	Reduces levels of prolactin, the hormone that stimulates milk secretion. The drug is used primarily to treat people with Parkinson's disease (85 percent of sales), who characteristically have greatly elevated prolactin levels due to a lack of dopamine, a chemical in the brain that suppresses prolactin. The drug is also used to suppress lactation following childbirth and in cases of elevated prolactin levels of unknown cause that may interfere with fertility.	

Drug*	Description
Lupron®**	Approved for use in Canada only in the treatment of prostate cancer. The drug suppresses testosterone production in the male and estrogen production in the female by inhibiting LH production. Approved in the U.S. for treatment of endometriosis (a condition that is estrogendependent), it is sometimes used in conjunction with IVF to suppress hormone production prior to starting a treatment cycle.

- * Names in parentheses are those of the manufacturer.
- ** Manufactured by TAP Pharmaceuticals, distributed by Abbott Laboratories.

New Drugs

At least five companies are known to be seeking approval to market fertility drugs in Canada. One is Organon Canada, which has filed NDSs with the HPB for two drugs. The products in question are similar to two Serono drugs but, according to Organon, are produced by a different method.

Alielix Biopharmaceuticals is developing recombinant (genetically engineered) versions of fertility hormones. Sandoz is evaluating a new drug for the treatment of infertility and other conditions associated with elevated prolactin levels. It is also studying the use of cyclosporin A to suppress the rejection of transplanted fetal tissue used in treating Parkinson's disease. The company describes this research as "very early and very limited."

Ferring is seeking approval for a drug called Lutrepulse[®], which is manufactured in Germany by Ferring and sold in the United States by Ortho Pharmaceuticals. This drug is an injectable product delivered by a battery-operated indwelling needle and a mini-pump worn by the patient. It is a synthetic product, chemically identical to gonadotropin-releasing hormone (Gn-RH), which acts on the pituitary gland to stimulate the release of LH and FSH, which in turn act on the ovaries. According to Ferring, the advantage over existing drug therapies is that Lutrepulse[®] is delivered in a "pulsed" fashion every 90 minutes, mimicking the natural hormonal secretory pattern. It is expensive, averaging \$1 000 per cycle.

Lutrepulse® was approved by the FDA in September 1990 and was first submitted to the HPB in May 1988. The company did not expect to receive final HPB approval within the following year.

Serono is engaged in developing recombinant fertility hormones and is currently seeking HPB approval for its growth hormone releasing factor (GHRF) for use in conjunction with infertility diagnosis. In addition, Serono

has filed a NDS for approval of a diagnostic product, gonadorelin (Relisorm[®]), used to evaluate pituitary function.

Sterling-Winthrop is researching a new delivery technology for Danazol®, a drug used to treat endometriosis.

Size of the Market for Fertility Drugs

Within the industry, the infertility market is seen as very small and of little interest by most companies. Industry statistics on sales volumes for the nine drugs listed in Table 3 would suggest that the market for fertility drugs in Canada is approximately \$9.3 million. However, IMS Canada, a company that gathers survey data on pharmaceutical product sales volumes based on hospital and pharmacy sales, readily acknowledges that data on fertility drug sales probably underestimate the market significantly. for several reasons. One is that survey data are more accurate for drugs that sell in large volumes, whereas fertility drugs generally sell in low volumes. A second factor is that data for drugs sold mainly through pharmacies are more accurate than data for drugs sold largely through hospitals. Fertility drugs are sold disproportionately by hospital clinics and hospital pharmacies and are not available at many retail pharmacies. In addition, drugs sold through private clinics are not captured in industry data at all, and there are a number of private fertility clinics in Canada that sell drugs to patients. Because of these factors, the market is almost certainly at least 50 percent higher than the \$9.3-million IMS estimate. Information provided by Serono Canada, the largest supplier of fertility drugs to the Canadian market, suggests that the total market is likely \$15 or \$16 million.

If \$16 million is used as the estimated market for fertility drugs in Canada and \$4.2 billion³⁸ for the total pharmaceutical market, fertility drugs represent approximately four-tenths of 1 percent of the pharmaceutical market in Canada. Sales of drugs for endometriosis are not included in the \$16 million figure. These drugs are used, to some extent, to treat infertility, but it is difficult to determine what percentage of endometriosis drugs are prescribed primarily to improve the fertility of the patient. IMS data suggest that the market for endometriosis drugs in Canada is approximately \$8 million.

The market for fertility drugs is dominated by one company, Serono Canada, a member of the Swiss-owned Ares-Serono Group. Serono is considered the world leader in infertility treatment; its drugs account for approximately three-quarters of the fertility drug market in Canada.

Other companies that produce drugs used to treat infertility regard the market as small and relatively unimportant. In the case of Sandoz, for instance, the infertility market accounts for only \$1 million of the \$9.3 million sales of its drug Parlodel[®]. Abbott's Lupron[®] is not approved for use in conjunction with IVF cycles, nor is the manufacturer seeking approval for that indication. Merrell Dow has relegated its product,

Clomid[®], which has been on the market for almost 30 years, to its non-promoted drug list, meaning that the company is doing nothing to advertise or promote the product; the company prefers to put its promotional efforts into products with a larger market potential. Ayerst's products, A.P.L.[®] and Factrel[®], are also not promoted.

Industry Views on Market Size

In general, industry representatives point to the small potential market as the reason companies are not more involved in producing and developing drugs to treat infertility. Other areas of women's health hold far more interest within the industry. Substantial industry funding is devoted to the area of reproductive biology, but it is directed to traditional fertility control (primarily) and post-menopausal therapies, according to Dr. Lawrence Russ, vice-president of Ortho Pharmaceuticals' Research Institute and board chairman of the Industrial Biotechnology Association of Canada (IBAC). "Companies tend to focus resources on areas where there are significant markets. If there's a major commercial opportunity [in infertility treatment], we haven't woken up to the fact. There are larger issues to deal with." The fact that generic manufacturers have not moved to manufacture the major fertility drugs (though the drugs are not under patent) also suggests that the market is not seen as sufficiently lucrative to repay the effort involved.

Dr. Pierre Major, vice-president of Scientific Affairs at Syntex, also commented on the size of the infertility market. The Syntex drug, Synarel®, used to treat endometriosis, is undergoing a clinical trial in Canada for use in conjunction with IVF cycles. But according to Dr. Major, this is not a significant area of pursuit. "It's peripheral. We're interested in endometriosis, so indirectly there's some interest [in infertility]. The [IVF] market potential is minuscule for us and minuscule for the industry as a whole. That's because it's a small segment of the population — women 30 to 40 who have infertility. A small chunk of a small chunk. If someone had said, 'we're going to develop Synarel just for IVF,' it would have never been developed, never."

Outside Canada, Roussel markets a product called Nemestran, a drug for endometriosis, but the company is not seeking approval to market it in Canada. Roussel president Don Buxton explained why: "There are already two or three products entering the market. The market is growing but it's not massive. So it's one of those difficult decisions we've been faced with. At the moment it's not a priority. We are involved in endocrinology and a lot of hormonal research but it's oriented towards the treatment of other conditions such as breast cancer and prostatic cancer. When you look at something like endometriosis, it's a very minuscule research emphasis of any company. Compare this with something like heart disease or hypertension. Nordic Laboratories sells \$100 million a year of [its heart drug] Cardizem. Clearly endometriosis is not in the same league."

PMAC Survey

Methodology

In late November 1991, Burson-Marsteller conducted a survey (Appendix 2) of all the members of the PMAC to elicit information about the companies' involvement in NRTs. The association assisted by sending a memo to its member companies advising them of the survey and urging their participation.

Twenty-seven companies (40 percent) responded to the survey; however, 10 answered by saying that none of the questions applied to them and therefore they would not be completing the survey in detail. Seventeen companies (25 percent) filled out the questionnaire, though not all responded to every question. Several answered only questions in Section A (on pharmaceutical products); many chose not to answer questions in Sections C and D (medical devices and STD kits). Serono Canada, the dominant company in the fertility drug market, is not a PMAC member and did not participate in the survey.

The PMAC advised consultants at the outset that many responses would probably consist of a long string of "no" answers, as most of the companies do not participate in the area of NRTs. Burson-Marsteller's own in-house survey/polling experts (Compas Research), who provided input into the survey design, advised that the typical response rate for this type of survey — of industry chief executive officers (CEOs) — is about 30 percent.

The following discussion summarizes company responses to key questions (for a more detailed summary see Appendix 3).

Findings

Only four companies responding to the survey said they currently produce drugs used in NRTs. One (Organon) is seeking HPB approval for two hormonal preparations; two (Syntex and Sterling-Winthrop) produce drugs used to treat endometriosis; and the fourth (Sandoz) markets a drug used primarily for other indications but also, to a limited extent, in infertility treatment.

Twelve of the 17 companies that completed the survey indicated they have no involvement in R&D related to NRTs. Of the five that are involved in R&D in this area, only one (Organon) described it as a significant part of its overall research program.

Question A.4 asked companies to comment on the market potential (for the industry as a whole) of drugs used to treat infertility. There was no consensus on this question, though the majority of respondents indicated that it is not a significant market. Three companies said the potential is significant; seven said it is not; one said it is moderate and another that it is "possibly" significant; the remainder did not know. Others indicated that it is a specialized or "niche" market, and therefore is significant to particular companies but not to the industry as a whole.

Nine companies provided substantive comments or suggestions on what role the government should take in regulating NRTs (question A.5). Comments tended to suggest that government should restrict itself to safety and efficacy issues and leave other questions to professional regulatory bodies. There were notable exceptions, however. Embryo research was singled out as requiring regulation. The need for standards of competence for assisted conception was also mentioned. One CEO commented that the field of NRTs is very new and therefore a cautious approach would be appropriate.

The most common response to question A.6, about the effect of increased government regulation, was that it would probably discourage R&D investment in Canada and increase costs.

Virtually all of the companies (13) that responded to question B.1, about the marketing of products used in genetic testing, said they are not involved in this area. Similarly, all 14 companies that answered question B.2, on involvement in R&D in the area of genetic testing, answered in the negative. Two mentioned that they use "genetic methods" or "biotechnology" but not in areas related to reproductive biology or genetic testing.

On the question of market potential for genetic testing there was no consensus, but responses leaned toward "large potential." Two companies said the market potential for genetic testing is large, and two said it is not large. Four said they did not know, and four provided comments such as "potentially large" and "could be large."

Two companies responded that they are involved in genetic *therapy* (as compared to genetic testing). One of these companies described its involvement as very "immature"; the other said it is applying molecular biology and recombinant DNA technology to "identify, isolate and sequence disease-causing genes and then introduce them into cells." Only four companies offered comments on the commercial potential of genetic therapy; their comments ranged from "mind-boggling" to "too early to characterize." (For a more thorough discussion of genetic technologies and the pharmaceutical industry's involvement in them, see Section 3.)

The two questions on the marketing of medical devices and diagnostics by affiliates of the pharmaceutical companies were poorly answered. Only two companies indicated involvement in the medical devices sector as it related to NRTs, both in diagnostics. Of the eight companies that responded to the question on potential market size for medical devices used in NRTs, six said they did not know or could not comment, one said the potential market is large, and the other said that it is limited.

All 10 companies that responded to the question on sexually transmitted disease (STD) test kits said they are not involved in producing such kits.

Conclusions from the Survey

Overall, the survey indicates that involvement of PMAC companies in NRTs is limited. Twenty-three of 27 companies (including the 10 that said the survey did not apply to them) indicated no involvement in the manufacture of pharmaceutical products used in NRTs. Only one company described this area as a significant part of its research program; that company is still seeking approval to market its fertility drugs in Canada.

The majority of companies that responded described the potential market for fertility drugs as not significant. Not one company said it manufactures products used in genetic testing, though several indicated a large potential market in this field. Two companies said they are involved in "genetic therapy," though it was unclear from their responses what sort of genetic therapy they were referring to. The section on medical devices and diagnostics was poorly answered and does not lend itself to meaningful interpretation.

It appears that the PMAC's prediction that the survey would garner mainly negative responses ("no, we're not involved") has largely been borne out. The results support information from other sources that infertility therapy is not a major area of involvement for the pharmaceutical industry. That said, it is recognized as a niche market for certain companies. In Canada at the present time, one company, Serono Canada, dominates the market.

Profile of Serono

Introduction

Serono Canada is a subsidiary of the Ares-Serono Group, an international developer and marketer of prescription pharmaceuticals, diagnostics, and over-the-counter products that is based in Geneva, Switzerland. Acknowledged within the industry as the world leader in infertility treatment, Ares-Serono also produces prescription drugs used in immunology and oncology, paediatric endocrinology, gastroenterology, and cardiology. The group operates subsidiaries in more than 20 countries and sells its products in 70 nations.³⁹

Serono's Canadian division was established in 1990 in Mississauga, Ontario. The company now employs about 20 people, including 7 salespeople who call on reproductive specialists across the country. Prior to 1990, Serono products were distributed in Canada by Pharmascience of Montreal. The Canadian company is a sales and marketing arm only; no drugs are manufactured in Canada. At present, drugs destined for the Canadian market are manufactured in the United States, Italy, and Israel. About 60 percent of Canadian sales are related to IVF. According to Serono, its decision to establish a Canadian affiliate was based on its desire to sponsor continuing education programs for health professionals in Canada and to support research in this country.

Internationally, Serono is the dominant producer of human fertility hormones (gonadotropins), including FSH, LH, and hCG. Its three leading fertility drugs are Pergonal® (a combination of LH and FSH), Metrodin® (FSH), and Profasi® (hCG). Other fertility products include Serophene® (clomiphene citrate), which acts on the hypothalamus to stimulate the release of FSH and LH, and a diagnostic test used to detect fertility disorders. The latter, a test of pituitary function, is not yet available in Canada but has been submitted to the HPB for approval.

Source of Drugs

The natural hormonal ingredients of Metrodin® and Pergonal® (FSH and LH) are extracted from the urine of healthy post-menopausal women aged 60 and over. Contrary to popular myth, nuns are not the main source; "there aren't enough of them," according to Serono. The active ingredient of Profasi® (hCG) is derived from the urine of pregnant women.

Research and Development

Ares-Serono's R&D activities centre on producing genetically engineered versions of natural hormone-based products. According to Serono's 1990 annual report, the group spent an average of 15 percent of net sales on R&D from 1986 to 1990. In 1990, its research investment worldwide amounted to US \$94.2 million. In Canada, the company spent approximately 5 percent of gross sales on R&D-related activities in 1990. (Serono is not a member of the PMAC and is not bound, therefore, by the association's commitment to increase R&D spending to 10 percent of sales by 1996.)

Present R&D efforts are focussed on producing the hormonal components of Pergonal[®], Metrodin[®], and Profasi[®], using genetic engineering techniques. These recombinant products are sought in order to eliminate dependence on the complex collection system currently used to obtain the natural raw materials, which are extracted from the urine of pregnant and post-menopausal women.

Genetically engineered FSH, now undergoing phase 3 (final phase) clinical trials, will be Serono's first recombinant product. Canada is expected to participate in these trials beginning in 1992. Research is also under way on recombinant LH, but this work is still a long way from clinical trials.

Ares-Serono maintains seven R&D facilities worldwide, including one in Boston devoted to fertility research. Globally, 16 percent of its staff are involved in research, and 15 percent of revenues are directed toward research. In Canada, Serono is supporting five clinical research studies at three teaching centres (Royal Victoria Hospital in Montreal, Ottawa Civic Hospital, and University Hospital in London). A Winnipeg hospital is also expected to become involved soon.

Four of the Canadian clinical research studies involve the use of Metrodin®:

- 1. in conjunction with GHRF in an effort to improve success rates in women who do not stimulate well on other drug protocols;
- 2. prescribed to patients with endometriosis;
- 3. prescribed to women with cervical (mucus) problems; and
- 4. in conjunction with intrauterine artificial insemination where there is a male factor.

The fifth study involves using Pergonal[®] in conjunction with GHRF to determine whether less Pergonal[®] may be required in that way. The company is doing work in the area of male infertility (one study each in Canada and the United Kingdom). Serono intends to broaden its "therapeutic scope" in coming years to include other reproduction-related disorders, such as menopausal dysfunction.

Educational Support

Last year, Serono spent \$600 000 to support R&D and educational programs in Canada. The company stresses the importance of funding continuing education symposia for allied health professionals as well as for physicians. Every two years, it sponsors an IVF nursing coordinators conference in conjunction with the World Congress on IVF. In the United States, it sponsors a certification review program for nurses — a course of study based on standards set by the American Nurses Association and other professional bodies. The company produces a wide range of educational booklets for patients, assists the Infertility Awareness Association of Canada to organize information seminars, and sponsors educational symposia and allied health programs in conjunction with the Canadian Fertility and Andrology Society annual conference. Serono advertises its products in medical periodicals.

Registry

Serono has provided funding to help establish a Canadian data base, or registry, to keep statistics on IVF and assisted conception. According to Jason Nestor, president of Serono Canada, the company provided \$56 000 after efforts by physicians to set up a registry foundered owing to a lack of funds. Serono is not involved in collecting the data; this work is being done by a U.S. firm using a computer program designed for Canada.

Serono Clinics

The Ares-Serono Group operates two clinics in Britain (in London and Cambridge) specializing in the treatment of infertility and assisted-reproduction techniques. Together, the clinics treat 5 000 couples annually. These were two of the first such clinics in the world. When they ran into financial difficulties a few years ago, Serono was asked to take over their administration to save them from bankruptcy. According to Serono, the clinics are not making a profit. A major function of the clinics is to serve as a training ground for health professionals. Serono benefits indirectly by having well-trained professionals working in the field. The

company has said that it has no intention of opening clinics in Canada or elsewhere.

Drug Prices

In Canada, Serono's drugs are sold through 15 to 20 wholesalers to hospitals and pharmacies. Normally, the drugs are not sold directly to doctors or clinics. Serono Canada purchases its drugs from the parent company and then marks them up for the Canadian market. The wholesalers boost the price again, as do the pharmacies. Pergonal[®], Serono's largest selling product, is sold to wholesalers for \$56 per ampoule. The retail cost to the consumer is approximately \$70 to \$80 per ampoule. Some hospital pharmacies are said to be selling it for only slightly more than the price charged by the wholesaler.

Pergonal[®], an injectable drug often used daily during IVF cycles (15 ampoules per cycle is average), is more expensive in Canada than in the United States — approximately \$4 per ampoule higher after correcting for the difference in the Canadian dollar, according to Serono. The company gives a number of reasons why the drug is more expensive in this country. Chief among these is the fact that drug batches destined for the Canadian market are manufactured in different locales than those destined for the United States. Pergonal[®] for the Canadian market is produced in Italy, while that for the United States is manufactured in Switzerland.

Canadian Pergonal[®] comes from Italy because of HPB requirements. In Canada, Pergonal[®] is classified as a biological drug. Biologics must meet more stringent standards than other drugs. HPB inspectors must inspect and license all manufacturing plants inside and outside Canada that produce biologics for the Canadian market. HPB inspectors travel to Italy on a regular basis to inspect the facilities that produce Pergonal[®] and Metrodin[®] for Canada. The United States does not classify these drugs as biologics.

Pergonal[®] destined for the Canadian market could not be produced in Switzerland (along with U.S. batches) because Switzerland would not allow Canadian HBP officials into the country to conduct plant inspections. According to Serono, this situation was resolved recently, but the Swiss plant is still waiting for a HPB licence.

Serono claims that Pergonal® for the Canadian market is more expensive than that produced for the U.S. market for the following reasons:

- 1. Batches are smaller and must be produced separately from U.S. batches (for the reasons described above). Since the size of the Canadian market is 7 percent of that of the United States, production costs of drugs for Canada are higher based on economies of scale.
- 2. Canada classifies Pergonal[®] as a biologic, whereas the United States does not. This classification means that Canadian manufacturing standards, quality control requirements, and

labelling are different from those in the United States. These differences add to the cost of production.

3. Corporate taxes are higher in Canada than in the United States.

Serono pays duty and brokerage fees on drugs brought into Canada, but no Goods and Services Tax (GST) or provincial sales tax.

Table 4.	Serono	Fertility	Drugs
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Drug	Year of First Notice Of Compliance	Manufactured for Canada in
Pergonal [®]	1967	Italy
Metrodin [®]	1987	Italy
Profasi [®]	Grandfathered*	United States
Serophene®	1986	Israel

^{*} On the market before the NOC system was established.

Source: Serono Canada. As naturally occurring substances, known hormones are not patentable. None of the Serono drugs currently on the market in Canada is under patent; consequently, their pricing does not fall within the jurisdiction of the Patented Medicine Prices Review Board.

Driving Forces in the Industry

It is clear from discussions with industry representatives that the predominant force driving the pharmaceutical industry is identical to that driving any other business or commercial venture — the need to make a profit on investment. Potential market size and profitability and the ability to develop an effective product within a reasonable time frame are the predominant factors in a company's decision to pursue a particular line of research.

Companies tend to find market niches, often producing a number of products in the same general classification or for treatment of a related group of diseases. This follows from the existence of established research programs and a base of scientific knowledge in a particular area.

Criticism of Pharmaceutical Industry Involvement in NRTs

During public hearings held across Canada in 1990, the Commission heard much criticism of the role played by the pharmaceutical industry in promoting and furthering new reproductive technologies. Numerous presentations and submissions by individuals and interest groups referred

to "huge profits" being reaped by pharmaceutical companies, along with charges that women are being exploited and subjected to "experimentation" for financial gain. Review of Commission hearings documents reveals several areas of concern about the activities of the pharmaceutical industry voiced by intervenors. These concerns can be grouped broadly under the following headings:

- 1. long-term effects of drugs;
- 2. lack of information available to women:
- 3. lack of research into causes and prevention of infertility;
- 4. corporate ownership of clinics;
- 5. exploitation of poor women from developing countries; and
- 6. "huge" profits.

These concerns are discussed below.

Long-Term Effects of Drugs

Concern has been expressed about the potential long-term effects of drugs used in IVF and other assisted-conception techniques. Questions have been raised about the adequacy of government (HPB) regulations and post-marketing surveillance. In addition, there are concerns about fertility drugs being used for non-approved indications or in doses that exceed recommended levels. Linked to concerns about long-term consequences are calls for a follow-up system or registry to track the long-term health outcomes of women involved in NRTs and of their children.

It is understandable that people are concerned about the use of drugs in conjunction with human reproduction when they are used in doses and for purposes that were never intended or fully investigated by the manufacturer. If this is happening (and there is evidence that it is), there appears to be an urgent requirement to evaluate the world literature on known long-term effects of the drugs and to assess the need for rigorous longitudinal studies, as well as for a follow-up mechanism (a registry and reporting system) to track long-term consequences. There are also concerns about the long-term effects of fertility drugs when used in recommended doses for approved indications.

It must be recognized that pharmaceutical companies comply with requirements, regulations, and standards imposed by external regulatory authorities. If there are concerns about long-term effects of drugs, it should not be anticipated that corporations will necessarily embark on longitudinal studies unless they are required to do so by the HPB. At the same time, pharmaceutical companies cannot be cavalier about the long-term effects of the drugs they produce; they need to be very concerned not only because of potential litigation, but also because their continued existence and profitability depend on their manufacturing and marketing effective products that win and maintain market approval. Concerns over

safety and reports of serious side-effects invariably harm a company's reputation and limit a product's viability in the marketplace or, as in the case of A.H. Robins' Dalkon Shield[®], eventually bankrupt the company.

As noted previously, several new drugs now under development are recombinant versions of natural hormone products currently marketed in Canada. It is to be hoped that the HPB will require that this new generation of drugs be subjected to rigorous evaluation of adverse and long-term effects prior to their entry onto the Canadian market.

Lack of Information Available to Women

A second major area of concern arises from the view that women are often not given adequate information about the possible effects of fertility drugs and are not always told when drugs are being used in doses that exceed recommended levels, for non-approved indications, or in "experimental" situations. In the absence of information from those responsible for their care (physicians, clinics, etc.), women must sometimes rely on the media or informal sources for information.

Clearly, there is a need for women who are considering taking fertility drugs to be provided with full information about the potential side-effects and long-term consequences of the drug therapy, both the pros and cons. Women should be told when drugs are being prescribed for non-approved indications or in doses that exceed recommended levels. The question is, "Whose responsibility is it to provide consumer information and to inform individual patients?" Under Canadian Food and Drugs Act regulations, the physician is considered the "learned intermediary" responsible for providing and interpreting information about drugs to patients and obtaining informed consent.

Many companies believe they have a responsibility, however, to provide patient information materials in the form of booklets, videos, and the like, made available through the learned intermediary. When they do, such materials cannot be seen to be "promoting" particular products, as manufacturers are prohibited from promoting prescription drugs directly to consumers. Such materials should provide complete and accurate information, unbiased in favour of "high-tech" solutions. It is not within the scope of this paper to critique patient information materials on NRTs distributed by pharmaceutical companies.

Lack of Research into Causes and Prevention of Infertility

Numerous individuals and groups pointed to a lack of funds for research into the causes and prevention of infertility. At least one intervenor at a Royal Commission on New Reproductive Technologies hearing suggested that pharmaceutical companies should be required to provide funding for research into the prevention of infertility equal to that used for the development of new drugs. There is concern, too, that pharmaceutical companies control research and that recent moves by the federal government to encourage linkages between basic researchers and

the private sector serve only to promote approaches to treatment that rely on drugs.

Pharmaceutical companies might argue that disease *prevention* is not their primary concern, except where pharmaceutical products are employed in prevention, as in the case of vaccines and antibiotics when they are used to prevent infection in an individual with a compromised immune system. Pharmaceutical companies are in the business of manufacturing and marketing pharmaceuticals, so they are unlikely to invest heavily in research directed at prevention unless such research is linked to the prospect of developing a marketable pharmaceutical or diagnostic product.

That said, it is important to realize that many drugs are used to inhibit the progress of disease, thereby preventing more serious problems. Antibiotics developed to combat certain STDs, for instance, may prevent infertility. Some companies incorporate a prevention message in their marketing approach. Syntex, for example, includes a condom in each of its Synphasic® birth control pill "starter packs" to encourage young women to use a condom in addition to the pill, to prevent the spread of STDs.

Many pharmaceutical companies do, in fact, conduct basic research aimed at understanding normal body processes (both at the cellular and functional levels) and discovering the underlying causes of disease or dysfunction. This understanding, while it may eventually lead to the development of new drugs, may also suggest methods to prevent or minimize the condition without drugs.

This dichotomy (research into causes and prevention versus research aimed at developing new drugs) may be an artificial distinction. It ignores a certain reality — that scientific research is an evolutionary process that often moves forward simultaneously on numerous fronts, including corporate research (basic and applied). Cross-fertilization among researchers in various settings (universities, hospitals, research institutes, and corporations) occurs through professional associations, national and international conferences, scientific journals, and informal professional networks.

Researchers in different sectors do not, as a rule, work in isolation. Often the first advances are diagnostic, then therapeutic, and finally, perhaps, preventive. This means that corporate research into underlying causes of disease in the course of discovering new drugs contributes to the larger body of knowledge about particular disease states or body systems. Ultimately, this work may lead to an understanding of prevention measures (as in heart disease) or to the development of drugs that prevent the progression of disease.

It is also important to recognize that research funded by pharmaceutical companies represents a relatively small proportion of all biomedical research done in Canada, though their R&D in this country is increasing. It is difficult, therefore, to see how companies can be said to control such research. In 1989 and 1990, for example, private industry funded only 8.3 percent of all biomedical research conducted by Canadian

faculties of medicine. More than 70 percent of such research was funded by federal and provincial governments and not-for-profit foundations. 40 Research institutes and hospitals also support biomedical research.

Corporate Ownership of Clinics

Another concern is that pharmaceutical companies may become involved in owning and operating IVF and assisted-reproduction clinics and thereby further commercialize reproductive technologies. As noted previously, the Ares-Serono Group, parent company of Serono Canada, took over the operation of two British fertility clinics on the verge of bankruptcy a few years ago. The facilities, two of the first such clinics in the world, serve as a training ground for health professionals. Serono claims that it does not make a profit on the clinics and has no intention of opening clinics in Canada or elsewhere. There appear to be no other major pharmaceutical companies contemplating ownership or operation of fertility clinics in this or any other country at this time.

Exploitation of Poor Women in Developing Countries

Concerns have been raised that experimental drugs are tested on women in developing countries under conditions that would never be permitted in more developed nations. It is generally acknowledged that such abuses may have occurred in the past; however, pharmaceutical industry representatives suggest it is highly implausible that costly pharmaceuticals such as fertility drugs would be tested in countries where the problem is controlling fertility, not overcoming infertility. The question is international in scope and has profound implications for developing nations. It is not within the purview of this paper to undertake a comprehensive review or analysis of this issue. To do so would require discussions with the World Health Organization and other international monitoring organizations.

Excessive Profits and Exorbitant Prices

An overriding concern of intervenors was the perception that pharmaceutical companies are making excessive profits and charging exorbitant prices for drugs used in conjunction with assisted reproduction. There is a sense that companies are exploiting desperate people who will do anything and pay any amount in their quest to have a child.

As described earlier in the paper, the market for fertility drugs is dominated internationally by one company, the Ares-Serono Group. The drugs are expensive — far beyond what most people could afford without the help of private drug benefit plans. One reason may be that the market for fertility drugs is relatively small. Serono offers a number of explanations as to why the drugs are so expensive and why they cost more in this country than elsewhere (see the subsection on drug prices in the section "Profile of Serono"). Certainly, the company claims that its profit margin is small. The real question is whether the price to consumers is justifiable based on the true costs of manufacturing and importing the

drugs. This question cannot be answered definitively here. However, the question is an important one and should be studied.

A General Comment

As noted earlier in this paper, the market for fertility drugs in Canada is very small, and the vast majority of pharmaceutical companies are not involved in this area. One company dominates the market. Two or three are involved in a very limited way, producing non-promoted drugs for small market niches or drugs used in conjunction with infertility treatment whose main uses are for other indications. A handful of companies are engaged in developing or seeking HPB approval for new drugs, most of which are equivalent or recombinant versions of existing drugs.

Much of the criticism of pharmaceutical company involvement in NRTs has been directed at the industry as a whole. It may be more appropriate, however, since the majority of companies have little or no involvement, to direct issues and concerns to the company or companies most directly involved.

Conclusions

While fertility drugs are expensive, it is clear that the market for these drugs in Canada is small (approximately four-tenths of 1 percent of the entire pharmaceutical market). Most pharmaceutical manufacturers have little or no interest in this market owing to its small size and highly specialized nature. It is, however, an important niche market for a handful of companies.

A single company, Serono Canada, dominates the market, with approximately 75 percent of total Canadian sales of fertility drugs. None of its products currently on the market in Canada is under patent, and therefore none is subject to the jurisdiction of the federal PMPRB. The fact that generic manufacturers have not moved to produce fertility drugs is a further indication that the market is not seen as sufficiently lucrative.

A number of the major fertility drugs have been on the market in Canada since the 1950s and 1960s; others were approved during the 1970s and 1980s. Several pharmaceutical companies are pursuing R&D in the area of infertility; however, most of the drugs involved are equivalent or recombinant versions of drugs currently on the market.

While there are concerns about the long-term effects of these drugs, responsibility for evaluating the need for longitudinal studies rests with the HPB. The new generation of recombinant fertility drugs now under development provides an opportunity to fully evaluate the adverse and long-term effects of these drugs before they are approved for sale in Canada.

Section 2. The Biotechnology Industry

Background

Biotechnology has been with us for centuries. The term refers to the use of biological processes and living organisms in the manufacture of products or as part of industrial processes. Wine-making is a good example of an application of biotechnology. Biological methods are employed in a wide variety of industries from aquaculture and mining to production of human and animal health products. Vaccines, for instance, are biological products that incorporate micro-organisms.

In recent years, biotechnology has become synonymous in the minds of many people with genetic engineering, the science of altering the genetic make-up of cells (often viral or bacterial) to produce customized biological products or a desired biological activity. Human growth hormone and insulin, now mass-produced in the laboratory, are examples of such products. They are manufactured by genetically altered bacterial cells into which the human gene for insulin or growth hormone has been spliced.

Biotechnology is used in many industrial sectors and is therefore, strictly speaking, not a discrete industry at all. Nevertheless, Canadian companies in many sectors that use biotechnology extensively have formed the Industrial Biotechnology Association of Canada (IBAC) to represent their interests. Within the health care industry, companies that specialize in using biotechnology to produce diagnostic and therapeutic products are often referred to as "biotech" companies.

As noted in the introduction to this paper, there is some overlap between the pharmaceutical and biotechnology industries. A number of traditional pharmaceutical companies employ biotechnology in research and manufacturing. Indeed, some of the major pharmaceutical firms have affiliates or research institutes that are members of the IBAC. Canada's largest biotechnology company, Allelix Biopharmaceuticals, is a member of both the IBAC and the PMAC (Pharmaceutical Manufacturers Association of Canada). Other biotech firms are small start-up companies and boutique operations.

Despite the amorphous nature of the biology sector, it is recognized by ISTC (Industry, Science and Technology Canada) as a "strategic" industry. ⁴¹ Together with the IBAC, ISTC has begun a five-year program to establish the Canadian Institute of Biotechnology to promote technology transfer and disseminate information to a wide range of industrial sectors that use biotechnology.

In 1983, the federal government established a National Biotechnology Advisory Committee, reporting to the Minister of State for Science and Technology, to recommend policies and strategies for the development of biotechnology in Canada. The advisory committee includes representatives from academia, government, industry, the general public, and the

investment community. It has established several working groups to develop recommendations for specific sectors of industry.⁴²

Companies

The Canadian Biotechnology Directory, 1990-91 lists approximately 270 Canadian companies and 30 research institutes from a wide range of industries. ISTC estimates that 300 to 400 Canadian companies could be included in the biotech industry. The directory lists companies according to the following categories, based on their principal activities and areas of research:

agriculture aquaculture consulting

diagnostics (animal and human)

energy environment

fermentation

food and beverage

forestry health care mining

pulp and paper

therapeutics (animal and human) waste water management

Some companies are listed in more than one category, but when overlapping listings are removed 94 companies fall into the health care, therapeutics, and diagnostics categories. A few companies are listed in all three categories and several are listed in two. About a dozen of the companies in the directory are major pharmaceutical manufacturers or research divisions of such companies.

A review of the descriptions provided by the companies about their business and research activities, technologies, and products (as published in the directory) reveals very limited activity related to NRTs. Only seven companies specifically mention R&D activities or products linked to human reproduction. These seven companies are listed in Table 5, with a brief description of their relevant activities.

According to Dr. William Cochrane, chairman of the National Biotechnology Advisory Committee and former CEO of Connaught Laboratories, work related to human reproduction or genetic testing is a "fringe activity" for the Canadian biotechnology industry. At the moment, there is very little activity by Canadian biotech companies in the area of genetic markers and test kits, "but I think you'll see it evolve within the next few years as a viable commercial activity. Clearly there's potential."

At the Biotechnology Research Institute in Montreal, a National Research Council Canada agency, Dr. David Thomas, head of Eukaryotic Genetics, said that in Canada there is virtually no private sector R&D into the kind of hereditary diseases that fall within the mandate of the Commission. "No one in Canada is involved. In the broad sense, yes — in the sense that genetic engineering work is the base [of much biomedical research]. But in the specific sense, the answer is no."

Table 5. Biotechnology Companies Involved in Areas Related to Human Reproduction

Company	Products
ADI Diagnostics	Diagnostic kits for detection of syphilis, Chlamydia, and gonorrhea
Alliance Medical	Research, development, and manufacture of ultrasonic diagnostics for detecting and assessing pregnancy
Cyberfluor	A new immunoassay system to test for certain biological substances and hormones including FSH, hCG, and prolactin; plans to develop a full line of fertility tests
Helix Biotech*	Purified proteins that are incorporated into test kits (by other manufacturers) for the early detection of birth defects; owns rights to gene probe technology used in paternity testing
Hospital for Sick Children Research and Development	Involved in trying to license the cystic fibrosis gene
Microbix Biosystems	Antigens used in laboratory testing for Chlamydia
Quadra Logic Technologies	Developing products for the treatment of STDs

^{*} Helix Biotech no longer makes any product related to genetic testing or detection of birth defects. It did previously produce proteins used in alphafetoprotein (AFP) testing, a biochemical test performed on maternal blood during pregnancy to detect fetal defects. The company discontinued making this product because of difficulty obtaining raw materials.

Source: Canadian Biotechnology Directory, 1990-91 (Ottawa: Winter House Scientific Publications, 1990).

Ying Gravelle, a business analyst with a science background, was with the Hospital for Sick Children (HSC) when she conducted a Science Council of Canada survey of Canadian biotechnology companies in 1989, to determine their involvement in genetic disease-related technology development and service delivery. That survey found that involvement by Canadian biotechnology companies in this area is very limited. Of the 30 biotechnology companies that responded to the survey, fewer than 10 were active in the development of specific diagnostic or therapeutic products for

genetic diseases. Those companies that were involved tended to focus on common single-gene and multifactorial disorders, such as cystic fibrosis, thalassaemia, muscular dystrophy, haemophilia, cancer, and cardio-vascular disease. The number of biotechnology companies found to be active in this area would have been even smaller if those working on therapeutics, as opposed to diagnostics, were removed from the group and if cancer and cardiovascular diseases were not included.

Many of the biotechnology companies listed in the *Canadian Biotechnology Directory* are involved in molecular biology and recombinant DNA work of various kinds, but almost none are engaged in the development of genetic screening tests or DNA probes for use in detecting human hereditary disease. A number of U.S. companies are involved in such work, however, and their involvement is discussed in Section 3.

The description of Allelix Biopharmaceuticals' activities, as described in the *Canadian Biotechnology Directory*, 1990-91, gives some indication of its pursuits:

The company employs over 75 scientific staff members, and operates primarily through collaborative efforts with academic researchers and joint ventures with established pharmaceutical companies possessing complementary clinical and marketing skills ... The company has developed proprietary technology to produce therapeutic proteins in a variety of recombinant systems ... and a major emphasis is the design of therapeutic molecules based on proprietary knowledge of specific drug receptors and technology.⁴⁴

Conclusions

Despite the common perception that biotechnology companies are a major force driving the development of technologies used in genetic screening, prenatal diagnosis, and research into gene therapy, this does not appear to be the case in Canada. In reality, exceedingly little such work is being done by the Canadian biotechnology industry.

According to academic researchers and scientists, Canadian research in this area is based in universities and genetics centres and is funded by government grants and private foundations. (Canada is known internationally for the high calibre of its research in this field; Canadian scientists have been responsible for a number of major breakthroughs.) In the United States, the private sector is involved in such pursuits, but even there, most basic science research in the hereditary diseases area is university-based.

Section 3. Genetic Technologies

Introduction

What is the commercial potential of genetic technologies — particularly those associated with screening for hereditary disease or used in prenatal diagnosis? What business interests are involved in commercializing these technologies in Canada and the United States?

The answers to these questions vary, depending on whom one talks to, on the current wave of market speculation, and on the amount of media attention being devoted to the latest breakthrough. As one corporate scientist with a U.S. biotechnology firm commented, "It depends on what year you ask — at times it's been overblown."

The following discussion is based on conversations with several senior Canadian scientists involved in genetics research, representatives of the pharmaceutical and biotechnology industries, and a number of business analysts in the United States and Canada. It concerns genetic technologies associated with the detection of hereditary disease through carrier identification, prenatal diagnosis (detecting fetal defects *in utero*), or (potentially) preimplantation diagnosis (testing the fertilized egg produced *in vitro* prior to transferring it back into the mother).

Not under discussion is the enormous body of molecular biology research and DNA technology (genetic engineering) employed widely in human health research and therapeutic applications — from detecting viral disease to producing better blood products (such work is not within the mandate of the Commission). Also not under discussion here, unless mentioned anecdotally, is another large body of research centred on discovering the genetic component of common multifactorial diseases, such as autoimmune disorders, Alzheimer's disease, cancer, and cardiovascular disease. The latter group is excluded because the use of detection tests for such conditions in prenatal diagnosis or reproductive decision making is considered a long way off and may never be feasible. Such tests may well be used, however, to make therapeutic decisions for adults with particular disorders in the near future.

Many of the large pharmaceutical companies are engaged in this genetic research into multifactorial diseases. Their interest lies not so much in the prospect of developing genetic tests (though they may do so in the process) as in the potential to develop new therapeutic drugs to treat individuals identified as vulnerable to these diseases. This area of research is viewed as having enormous potential for the pharmaceutical industry.

Basic research into that group of disorders traditionally thought of as hereditary diseases (cystic fibrosis, Duchenne muscular dystrophy, Huntington's disease, etc.) is aimed at gaining a better understanding of the genetic basis of the disease by identifying the gene or genes responsible and pinpointing specific mutations. The driving force at the academic level (where most of the basic research is done) is not primarily the development

of screening tests to identify carriers or affected individuals, but, rather, the hope that an effective treatment may be found once the disease is better understood.

In the course of this work, DNA probes (complementary strands of DNA that "recognize" specific DNA sequences contained in a test sample) and markers (similar to probes) are developed and used to detect the gene responsible for a particular disease. Testing methods using DNA probes are often technically complex and very expensive and can be performed only under the supervision of a highly trained scientist in a university research setting.

The commercial challenge is to develop simple, accurate, inexpensive tests that lend themselves to wide use in the hands of lesser-trained technologists. This technology transfer is no mean challenge. At present, several U.S. biotechnology companies are trying to develop DNA-based (molecular) cystic fibrosis tests for use in mass screening, but because the gene is very complex (with 140 mutations identified so far) and a different probe is required for each mutation, the quest is expected to be long and costly.

The commercial potential of such scientific discovery depends directly on the complexity of the science, whether it can be applied practically, and how profitable it would be. Is there a large commercial potential in these technologies? On this question, there is no consensus. Virtually all the scientists and corporate representatives questioned acknowledged that there is some commercial potential for genetic testing, if and when inexpensive and highly accurate tests can be developed that are suitable for commercial screening purposes. It is considered very unlikely, however, that mass screening will ever be introduced for diseases with very low incidences (for example, 1 in 50 000), for reasons of cost.

Several major questions were identified that must be answered before screening becomes commonplace (and before investors will take the risk of commercialization). One is, who will pay for expanded genetic testing programs? At present, testing is not available in commercial laboratories in Canada. It is done only by laboratories associated with university teaching hospitals or hospital-based genetics centres, such as the nine regional genetics centres in Ontario. Testing is expensive and requires trained counsellors to interpret the tests to patients and provide information about options.

Even if costs come down, the question remains as to whether provincial health care plans will agree to fund expanded screening and counselling programs in this day of shrinking health budgets. Even more problematic are the ethical issues, including the fundamental question, "Is this something we want to be doing?" Such questions have a dampening effect on investor enthusiasm.

In spite of uncertainties, there appear to be three potential areas of commercial opportunity in genetic testing. One is in "discovering" a gene

and patenting it, the second is in developing practical screening tests, and the third is in providing testing services in a commercial laboratory setting.

Patenting Genes

The Hospital for Sick Children (HSC) in Toronto has had some experience in patenting genes, but so far these efforts have not paid off. Several years ago, HSC researchers identified and characterized the gene for Duchenne muscular dystrophy (as did another group in the United States) and decided to try to patent some feature of it.

"Nobody thought it was going to make a huge amount of money," commented Dr. Ronald Worton, HSC geneticist-in-chief and associate director of the Genetics Network, Centres of Excellence, a federal government program to link academic researchers with industrial partners to facilitate technology transfer. "The hospital put a big effort into it, so did the Muscular Dystrophy Association. We spent \$20,000 to \$25,000 trying to develop the patents and have now given them up. We don't think there's enough commercial potential and we've dropped them. It costs a lot of money up front to patent something. When we began to look at the potential market and anticipated payback, we found it would take many years just to recover the initial investment. Now the test is being used around the world and we're not making a cent. Several companies have picked it up, and I imagine, are making a little money."

The hospital is hoping for better success in patenting the sequence for the cystic fibrosis gene, discovered by HSC scientist Dr. Lap-Chee Tsui in 1989. So far, the hospital has spent over \$100 000 on efforts to patent the gene (with help from the Cystic Fibrosis Foundation). It expects to start licensing the technology to companies interested in developing commercial tests as soon as patent pending status is granted. Normally it takes three to five years to obtain a patent, and companies are not required to pay royalties to the innovator until the patent is issued.

The scientific information about the cystic fibrosis gene has been published and is in the public domain. Several U.S. companies are already using it for testing purposes, but they are not paying royalties. Once royalties start coming in, the hospital expects it will take two to three years to recoup the patenting costs. The royalty is a percentage of the selling price of the test, so revenues depend on how much the test sells for, which at this point is unknown. Costs will be recovered only if an inexpensive, widely used test can be developed. The HSC will share royalties with the University of Michigan, which contributed to the discovery.

"The reality is," said Dr. Worton at the HSC, "that there have been very few windfalls in the area of genetic testing." A possible exception is the original DNA probes developed in Great Britain and used for forensic purposes (often called DNA fingerprinting). Similar technology is now used in paternity testing.

Developing Genetic Tests

In the world of genetic testing there are many different types of tests. The most widely available and traditional kind of testing is cytogenetics, which involves culturing cells (fetal cells obtained by amniocentesis, for example) and studying the number and appearance of the chromosomes. Another is biochemical testing. The principal biochemical test used in prenatal diagnosis is AFP, which detects the level of this fetal protein in the mother's blood or amniotic fluid. An abnormally high or low level may indicate a problem with the fetus.

The newer DNA-based tests (often referred to as "molecular genetics") identify the presence of specific DNA sequences within a gene. There are different generations of DNA diagnostics. As noted previously, first-generation tests are labour-intensive and very expensive and can be used only in the hands of highly trained scientists and technologists. These kinds of tests are being used in research centres, in some hospital laboratories, and, in the United States, in a small number of laboratories operated as commercial businesses. But the tests have not yet been perfected. U.S. commercial centres, for example, are testing for only a handful of the most common of the 140 known cystic fibrosis mutations, according to Dr. B. Handelin of Integrated Genetics in Massachusetts. The challenge now is to develop very accurate, inexpensive screening tests; this is where the commercial sector comes in.

For Barbara Lavers, technology licensing manager at the HSC, the biggest problem is trying to interest companies in commercializing this kind of technology, because "there isn't enough money in it. Companies aren't going to invest in a project without some expectation of profit." According to Lavers, commercial development costs can be five to ten times higher than the cost of the basic science.

The cystic fibrosis gene may be the exception. It has generated considerable commercial interest owing to the fact that cystic fibrosis is the most common genetic disorder among Caucasians -1 in 20 is a carrier.

Several U.S. firms are trying to develop screening tests suitable for commercial use. What sort of pay-back is likely for the company that perfects such a test and gets it to market first? According to David Steinberg, a market analyst with the Manhattan investment research firm Mehta and Isaly who follows the biotechnology industry, "The big profits are in therapeutics, not diagnostics. Diagnostics can be profitable if you do them en masse. But you have to run a lot of tests to make it worthwhile. Lots of research is being done at the university level, but in terms of commercialization, [genetics testing] is a minor area for the biotech industry. Individual companies have a small niche."

Commercial Genetic Testing

The total current U.S. market for all types of genetic testing has been estimated at approximately \$50 million annually, according to Matthias

Duys, vice-president of sales and marketing for Vivigen, the largest U.S. company specializing in genetic testing. Average profit margins within the industry are in the 30 to 40 percent range, he indicated. Vivigen, based in Santa Fe, New Mexico, does not conduct original research but acquires technology and adapts it for use in the commercial laboratory setting.

The industry is dominated by five or six companies that work exclusively in the genetics testing field and three or four others that offer genetic testing as well as other kinds of clinical testing (the largest being Roche, SmithKline and Metpath). In addition, there are about 200 smaller companies in the business. "It's a growing industry and will grow even more because of the work that's going into the human genome project," commented Duys. "The impact will be huge in terms of being able to assess our individual make-up or our predisposition. The questions are mainly ethical — what are we going to do with this information, use it or abuse it?"

Asked whether Vivigen has looked northward to the Canadian market, Duys indicated that the market is of interest, but there are some limitations on sending specimens in and out of the country, and there might be some pricing issues. "But the market is large and I'd like to tap into it."

Integrated Genetics (IG Labs) of Framingham, Massachusetts, a subsidiary of Genzyme, is another major player in the genetics testing business. It operates four commercial laboratories in the United States, one of which began doing DNA diagnostics commercially in 1986. All four do standard cytogenetics testing. Dr. Barbara Handelin, director of molecular genetics diagnostics at IG Labs, estimated there are about 6 commercial and 30 university-based DNA diagnostics laboratories in the United States. None is doing screening on a mass scale because the technology is not available.

Dr. Handelin estimates that approximately 15 000 to 20 000 DNA-based tests are now done yearly in the United States. Each test costs \$150 to \$300. What are the market projections if the tests become simpler to do and the costs come down? This is the key question, but no one really knows how interested people with no family history of genetic disease are in having information about their personal genetic risk factors. To find out, six pilot cystic fibrosis screening studies are under way across the United States, funded by the National Institutes of Health. Through this work, researchers will also gain experience in doing large-scale testing.

At IG Labs, some testing is done at a loss, with high mark-ups on other tests to cover costs. Testing for Huntington's disease, for example, has to be done by a very laborious method because the gene has not yet been cloned. It takes two weeks to complete the tests, and the procedure is very labour-intensive. The cost of doing the tests is \$675 per individual (several family members must be studied), but patients are charged \$495. Cystic fibrosis testing, on the other hand, costs a little under \$100 at current volumes, but patients are charged \$150 to \$230 each.

Dr. Handelin estimated that the price could come down to \$65 or \$70 with higher volumes and may eventually be \$35 or \$40.

IG Labs is also doing leading-edge research in fetal cell separation and *in situ* hybridization, which together could potentially revolutionize prenatal diagnosis, opening the door to routine prenatal genetic assessment. Fetal cell separation refers to a technique whereby fetal cells are extracted from maternal blood, thereby reducing the need for amniocentesis, an invasive procedure. *In situ* hybridization may one day enable quick, efficient assessment of fetal cells without time-consuming culturing (growing) of cells. Fetal cell separation is at least five years away from clinical testing. It would most likely be used as a screening test, followed by amniocentesis if abnormal results are found. The company's attitude toward cost is that the test must be offered for under \$100 or it will not be widely used.

The Driving Force

There is no question in Dr. Handelin's mind about what is driving the genetics testing industry. "It's the science that's driving it, because both the technology is moving quickly and new ideas about how to analyze the human genome are coming fast and furious from all over the place, mostly from outside the industry. Genetic disease has really lagged behind other areas of medicine in terms of being able to do anything preventive or interventive. Now there's a big drive to be able to do something for people." Private foundations, such as the Cystic Fibrosis and Muscular Dystrophy foundations, established by individuals concerned about these diseases, are also major driving forces and raise money for research.

Recently, IG Labs started offering testing for spinal muscular atrophy, the first time prenatal diagnosis has been available for this disease. The drive to do it came from families who had been calling the lab for over a year asking when it would be available. "We were saying, 'we're not quite ready, the test is not perfected,' and they were saying 'we don't care if it's

not perfect, we want it'."

The other kind of testing for which there is expected to be a large market is testing for predisposition to various common disorders such as cancer and cardiovascular disease. "This has a very large potential but will be limited by the value physicians place on having more accurate information about which patients are at high risk," commented Dr. Handelin. It will also depend on the value consumers place on knowing their risk factors ahead of time, and this will depend to some extent on whether effective treatment methods are available.

Dr. Handelin estimated that we are only three to five years away from having diagnostic tests for predisposition to some types of breast cancer and cardiovascular disease. In the Canadian health care system, the most important limitation may be the willingness of provincial health care plans to cover the cost of such testing.

The Canadian Situation

According to Dr. Worton at the HSC, there is no commercial genetics testing being done in Canada. Asked whether industry is driving these technologies, he said, "From our point of view, the problem is exactly one hundred per cent opposite to the picture that has been painted. We've had trouble in Canada getting good companies even interested in genetic testing for common genetic disorders, because there's not enough money in it. In the U.S., it's a little different. There you can open up shop and offer diagnostic testing."

These views are shared by Dr. Charles Scriver, director of the deBelle Laboratory for Biochemical Genetics, McGill University-Montreal Children's Hospital Research Institute: "In this country nothing much is happening [in terms of commercializing genetic technologies] because there's no purchaser. [The provincial health care plan] doesn't pay for a single biotech thing in our program here at McGill. All the new technologies are funded out of research grants and a small bit of funding from the Quebec Medical Research Council. [Our people] are so frustrated at the lack of funding that they're actually funding service provision out of R&D at the present time. That's fairly true across the country. Companies aren't going to be able to make any money in Canada — they'll be able to sell to the U.S., but the market doesn't exist here."

Dr. Worton is concerned that we are on the verge of an explosion in genetic technologies and vastly increased consumer demand, which the existing system could not possibly cope with. "We've always argued that the testing is not routine enough [to be done commercially]. It's constantly changing and evolving and getting better and as long as it's in that phase, it's better off in a hospital. But as soon as it gets to the point where it's cheaper, more stable and higher volume, then I think it's time to move it off to the commercial labs."

Recently, Dr. Worton and Dr. David Shindler, managing director of the Canadian Genetic Diseases Network, federal Centres of Excellence program, took a first step in attracting a commercial player to the genetics testing field. MDS Laboratories, Canada's largest laboratory services company, has agreed to fund a pilot cystic fibrosis screening project in Montreal as part of the Centres of Excellence program. This partnership will give the company a window on scientific developments in the field and an opportunity to assess future commercial potential.

"We've talked to [MDS] for four or five years now and they're interested but they're looking at what's happening in the U.S. and saying, 'we're not going to jump into this because we may lose money'," commented Dr. Worton.

According to him, the best chance for commercialization may lie in "multiplexed" tests. If a good, rapid, efficient, inexpensive test for cystic fibrosis were developed, for example, other tests could be "piggybacked"

onto it. Instead of doing just one test, a whole battery could be done using the same blood sample.

Researchers point to the results achieved in Cyprus when a universal screening program was introduced for thalassaemia, a debilitating, not readily treatable blood disorder that has a high incidence in the local population. Before the screening program was introduced, about 70 babies a year were born with the disease, but after two or three years of screening, the incidence dropped to approximately 2 a year (women carrying affected fetuses were offered termination of the pregnancy). "With cystic fibrosis you could imagine a similar sort of thing, if you screened the whole population," noted Dr. Worton. "The question is not who's going to make how much money, but is this something we should be doing?"

In Canada, the relative priority of such a program among competing priorities and the willingness of health ministries to fund it would be important determining factors.

The Pharmaceutical Industry and Genetic Technologies

For the most part, pharmaceutical companies are not involved in a major way in the genetic technologies of relevance to reproductive technology, with certain notable exceptions. In the United States, for instance, Abbott Laboratories is involved in developing instrumentation and automated sample processing for genetic testing. Roche Biomedical Laboratories operates genetic testing services.

As noted previously, many of the large pharmaceutical companies are conducting extensive research into the genetic origins of multifactorial diseases such as cancer and heart disease. Their prime motivation in doing so is to develop new therapeutics based on an understanding of the molecular basis of the disease.

The day when tests for common multifactorial diseases may be used in prenatal diagnosis and reproductive decision making is considered by most experts in the field to be a long way off. Some people question whether tests for such diseases will ever be used in prenatal diagnosis, because the diseases are common and generally do not affect people until mid-life. By the time accurate tests become available, it is likely that better understanding of underlying disease processes will have led to ways to avoid expression of the disease. It is questionable, therefore, whether prospective parents would want to use prenatal screening to select against such conditions and whether society would accept it.

Some pharmaceutical companies are involved in making recombinant drug products for use in reproductive biology. One current example is Genentech, which is in clinical trials with its new drug Relaxin, a recombinant version of a naturally occurring substance that causes the cervix to soften during childbirth. If this drug proves successful, the hope is that it will help reduce the need for Caesarian section. At least two other

companies (Serono and Allelix) are known to be developing recombinant versions of fertility drugs now on the market.

By and large, pharmaceutical companies are not involved in doing basic genetics research, though a few are funding such research. Bristol-Myers Squibb, for instance, has given \$5.7 million to the Mount Sinai Hospital Research Institute in Toronto to do research using transgenic or mutant mice (i.e., mice into which foreign genetic material has been introduced) to develop models of genetic disease. The researchers will try to create a cystic fibrosis mouse, according to Dr. Lou Siminovitch, director of the institute. "Ninety to 95 percent of this kind of research is university-based," he noted. "One source of funds is the Medical Research Council, another is the private foundations."

The Medical Research Council's University-Industry Program currently provides \$7.5 million to approximately 140 projects across the country, matched by \$9 to \$10 million in industry contributions, according to Dr. G. Beauchemin, the director of the program. Program officials review research being done in university faculties of medicine and pharmacy and attempt to match this with the research interests of pharmaceutical companies. Very few of the projects involve genetic research of the kind that falls within the mandate of the Commission.

Conclusions

At the present time in Canada, there appears to be very little private sector R&D in those areas of genetic technology specifically within the mandate of the Commission. However, considerable research of this kind is being conducted at universities and research institutes, funded by government and charitable foundations.

This reality contradicts the common perception that extensive research of this type is being done within the pharmaceutical industry. Globally, pharmaceutical companies are, in fact, involved in a great deal of genetic research, but, for the most part, their work is directed at discovering the molecular basis of common multifactorial conditions such as heart disease and autoimmune disorders. Their goal is to develop new drugs once these diseases are better understood, not to develop genetic tests.

In the United States, several biotechnology companies are trying to develop screening tests for common hereditary diseases. It is not yet known, however, how much interest people with no family history of genetic disease have in knowing their genetic risk factors. Commercial genetic testing in the United States is a \$150 million business and growing. In Canada, however, there is currently no commercial genetic testing; all such testing is done by hospitals, universities, and genetics centres funded by government. Future availability of genetic testing in this country will depend largely on the willingness of provincial health care plans to pay for testing and to provide essential counselling.

Scientists and industry representatives generally agree that genetic screening and testing have commercial potential. However, the magnitude of that potential will depend on the willingness of governments to fund testing programs and on ethical considerations. Until these issues are resolved, commercial involvement in Canada is likely to be limited and tentative.

Overall, the greatest profits in genetic technologies are likely to be realized by companies that perfect simple, accurate screening tests for common hereditary diseases and those that develop effective drugs to treat or suppress multifactorial conditions that have a hereditary component.

The driving force behind development of genetic technologies appears to be the rapid evolution of scientific knowledge in this area coupled with the desire of families that suffer from hereditary disease, and their doctors, to finally be able to do something to treat or prevent hereditary conditions.

Section 4. The Medical Devices Industry

Overview

ISTC (Industry, Science and Technology Canada) defines medical devices as "health care products used for diagnostic or therapeutic purposes which are not drugs or medicines." The medical devices industry in Canada is made up of approximately 650 companies selling products in 6 500 categories, ranging from gauze bandages to magnetic resonance imaging equipment, medical information systems, laboratory reagents, and ovum aspiration needles used in IVF. It is a \$2.5 billion industry based mainly in Ontario and Quebec and employing 10 000 people. Eighty percent of products destined for the Canadian market are imported, largely from the United States. 50

MEDEC (Medical Devices Canada), the industry's trade association, represents about 100 medical device suppliers in Canada. MEDEC defines the main subsectors of the industry as diagnostics, medical imaging and therapy, medical/surgical supply, hospital equipment, implants, and assistive devices. There are up to 300 000 different products on the market in Canada (including 837 kinds of sutures), which makes classification a problem. The FDA (Food and Drug Administration) in the United States has adopted a complex classification system based on medical disciplines, but according to MEDEC, the industry tends to classify these products along manufacturing lines.

The Canadian industry is dominated by a number of large multinational companies, but it also includes many small and medium-sized firms. Most of the multinationals manufacture products in Canada for the domestic market but do not export Canadian-made products to the world market. Canada, on the doorstep of the world's largest market for medical devices, manufactures only 1.5 percent of world production. The

U.S. market for medical devices (\$25 billion in 1988) represents 59 percent of world demand.⁵²

ISTC, as part of its *Meeting the Challenge* initiative, is targeting the medical devices industry as one capable of significant growth during the 1990s. World demand for medical devices is increasing rapidly, and some subsectors and niche markets are growing exponentially. According to ISTC, Canada is well positioned to become a significant player in the world market but has not yet fully exploited that potential. "It is not unreasonable to expect that the Canadian industry could grow to a multibillion dollar industry by the year 2000." 53

A senior ISTC official, Dr. G. Michaliszyn, believes the low-technology end of the industry is starting to disappear in Canada. It is becoming a very cost-competitive business and is rationalizing globally, with production of low-cost, commodity-type products moving out of Canada.

Medical Devices in NRTs

Medical devices with most relevance to NRTs include diagnostics (used in laboratory testing to measure various hormone levels), ultrasound (used daily in some IVF cycles), and specialized equipment designed for ovum retrieval, embryo transfer, artificial insemination (AI), and related procedures. Also included are test materials and equipment used in cytogenetics laboratories.

Industry representatives say it is not possible to measure the segment of the medical devices industry devoted to NRTs, but it is considered to be very small. According to Phil Nance, president of MEDEC, there is recognition within the industry that certain specialized items are used in connection with IVF and other NRTs, but the subsector is so small it is rarely mentioned. It is possible, however, to look at specific items and estimate the size of those markets.

Diagnostics and Commercial Laboratory Testing

There are two commercial opportunities in laboratory testing — one is "diagnostics," the other is the provision of commercial laboratory services.

Diagnostics involves producing and selling test materials (reagents) consumed in the process of laboratory testing, as well as developing and marketing the computerized auto-analyzers and other sophisticated equipment used to process test samples. Typically, the larger diagnostics companies (sometimes divisions of major pharmaceutical manufacturers) produce both the reagents and the processing systems used in testing. Smaller diagnostics firms may sell only specialized lines of reagents.

The second major commercial activity is the provision of commercial laboratory services. Commercial labs are not, strictly speaking, part of the medical devices industry but are discussed here because they are related to the industry and relevant to NRTs.

Diagnostics

Phil Nance of MEDEC estimates that approximately 200 companies in Canada supply the domestic diagnostics market. About 15, including a few giants, share 80 percent of the market. Only 20 percent of the diagnostics for the Canadian market are made in Canada, and much of that share is manufactured by Canadian divisions of multinationals.

The total Canadian market, including sales of equipment, instrumentation, and other capital items, and of consumables (reagents, test materials), has been estimated at \$600 million. This figure is considered high by some industry observers; estimates depend on what is included in the category. There is some agreement, however, that \$350 million is a reasonable estimate for the consumables portion of the market.

Reproductive endocrinology tests used most frequently in conjunction with infertility assessment and assisted-conception techniques are those to measure estradiol, LH, FSH, and progesterone. Sales of these tests were one of the fastest growing segments of the diagnostics market during the 1980s but still represent a very small share (approximately 2 percent). Despite a major marketing thrust in developing reproductive tests during the 1980s, they remain one of the smallest revenue centres for most diagnostics companies, according to Darrell Skelly of Livingston Pharmaceutical Distribution.

"Reproductive testing is not a big money spinner for diagnostics companies," noted Skelly. "It's an add-on so as to provide a full range of tests. There are a few small companies for whom it's their lifeblood but it's minuscule in the industry. I think you're going to find that these kinds of tests make up less than two per cent of diagnostic product revenues."

Nevertheless, 2 percent of \$350 million is a \$7 million market, not insignificant for some niche companies.

Commercial Laboratory Testing

Commercial laboratory testing services (as distinct from diagnostics) constitute a \$425 million industry in Ontario, according to Paul Gould, executive director of the Ontario Association of Medical Laboratories. Unfortunately, there is no national association of such businesses, and Ontario is the only province with a provincial body. In the other provinces, the provincial medical associations perform many of the functions carried out by the Ontario Association of Medical Laboratories, such as negotiating the schedule of benefits with government on behalf of commercial labs. The lack of a national association makes statistics hard to collect. For this reason, the discussion below is based mainly on data extrapolated from Ontario information.

One way to estimate the Canadian market for commercial lab testing would be to simply multiply the Ontario figure by three, given that Ontario has approximately one-third of Canada's population. However, the resulting figure of \$1.35 billion is probably far too high, as three of the

Atlantic provinces have no commercial laboratories. All lab testing in those provinces is done by hospital or government labs. Commercial testing in some other provinces is limited. One source estimates the appropriate multiple is more likely 1.5, giving a figure of \$675 million. Others suggest this number may be low. For lack of any better number, we will "guesstimate" the market at \$700 million.

Clinical diagnostic laboratories provide lab testing in biochemistry, haematology, cytology, pathology, and, theoretically, cytogenetics — except that no private labs are licensed to do this last kind of testing (see Section 3). Approximately 600 laboratory tests are listed in the Ontario schedule of benefits.

Commercial laboratories in Ontario are licensed under the Laboratories and Specimen Collection Centres Act, administered by the Ministry of Health. In that province, private labs must participate in a laboratory proficiency testing program administered by the Ontario Medical Association. Blind samples are tested, and the results are screened for accuracy ("proficiency" is the term used). Laboratory services performed by doctors in their own offices are an exception to this process; physicians do not need a licence, nor are they required to participate in the proficiency program. This practice is causing concern for two reasons: (1) some doctors are using lab testing as a means to increase revenues as caps are placed on physicians' incomes; and (2) quality assurance may be a problem. This phenomenon may have implications for reproductive biology clinics, where doctors have tended to set up their own labs.

The Ontario Association of Medical Laboratories (OAML) has 25 corporate members representing 80 percent of private laboratories in the province. It does not represent hospital laboratories (funded out of global hospital budgets) or public health laboratories. Four companies (MDS Laboratories, DynaCare, Med-Chem Laboratories, and Excel-Bestview) dominate the market with 70 to 80 percent of market share. ⁵⁶

There is some private payment in the laboratory services business (insurance medicals, employee health screening), but Paul Gould of the OAML estimates that 99.9 percent of revenues are generated by lab tests performed as insured benefits under provincial health care plans. Some commercial laboratory companies have contracts to manage hospital labs, though this is uncommon. Companies compete to serve the physician community on the basis of turn-around time, accuracy of tests, quality of reports, and availability of consultation for interpretation of results.

The industry association in Ontario has developed a code of ethics, which member companies are obliged to follow. In the past, the industry has been hurt by the unethical practices of some companies and some doctors. Doctors, for instance, may have received reduced rent in a medical building owned by a lab company in exchange for sending patients for lab tests. Under the code, it is unethical for companies to pay for referrals or to offer doctors other inducements. Equipment and supplies provided by a lab company to doctors free of charge must be for the purpose of

obtaining and maintaining specimens for testing. In the case of computers, free equipment must be hooked up to receive lab results. Currently, the industry association and the Ontario Medical Association are working on joint guidelines to govern their mutual relationship.

There are a number of important issues facing the industry. One is the rate of increase in the use of lab services. In Ontario, laboratory services (commercial, hospital, and public health) are estimated by Robert Pharand of the Ontario Ministry of Health to consume \$1 billion of the \$17 billion health care budget. Of course, laboratories do not order tests, physicians do. Laboratories are responsible for carrying out tests on the written request of a physician and are paid by the government for doing so.

In Ontario, the Ministry of Health has taken what the association terms a "simplistic" approach to the problem by cutting back payments for lab tests by 5 percent across the board, effective January 1992.

Commercial Laboratory Testing and NRTs

Dr. Tom England, laboratory director with MDS Laboratories, Canada's largest laboratory services company, attempted an estimate of the size of the commercial laboratory market for testing related to infertility and assisted-conception techniques. As mentioned previously, the main tests used are for estradiol, LH, FSH, and progesterone; there are others, but these four account for the bulk of testing. Considerable hCG testing is also done in connection with IVF and other assisted-reproduction techniques to confirm whether implantation has occurred. It is not possible, however, to separate out the proportion of hCG testing done in conjunction with IVF and assisted conception from that performed to confirm normal pregnancy.

Dr. England's estimate is based on the MDS experience in Ontario, where the company has one-third of the market for commercial testing. He believes the market for estradiol testing (the most frequently done test, performed daily during ovarian stimulation) in Ontario to be approximately \$1.5 million annually; for the other three tests together, it is approximately \$2.25 million. To estimate the total for Canada, we multiply the Ontario total (\$3.75 million) by two (instead of three, because it is probable that more of this testing is done in Ontario than in the rest of the country, since Ontario has a greater number of infertility clinics). Based on this calculation, the size of the commercial market for infertility testing in Canada is roughly \$7.5 million.

Testing related to IVF and assisted conception accounts for 1 to 2 percent of MDS revenues, according to Dr. England. The tests are expensive (the Ontario Health Insurance Plan reimburses \$25 to \$30 for each test) but are profitable for laboratories only if done in large volume. The volume of infertility testing conducted by the private sector increased during the 1980s but now appears to have levelled off, owing at least partially to the fact that doctors in IVF clinics have incorporated lab testing into the services they offer.

Ultrasound

At one time, ultrasound in obstetrics and gynaecology was used mainly in assessment of pregnancy, but now the procedure has evolved far beyond that. Today ultrasound is used routinely in investigations related to infertility (to visualize the uterus and fallopian tubes, for instance) and daily during IVF and some assisted-conception cycles to monitor follicular development.

According to Margarita Reti, president of ResCan Consultants, a Montreal firm that tracks hospital sales of medical devices across Canada, the market for ultrasound equipment in Canada is approximately \$50 million — \$32 million in hospital sales and the remainder in government labs, university research centres, and doctors' offices. However, Phil Nance of MEDEC believes the ultrasound market in Canada is considerably smaller. No reliable data is available on the percentage of ultrasound equipment used in conjunction with NRTs.

Devices Used in IVF and Assisted Conception

A number of specialized devices have been developed specifically for use in IVF, AI, and related procedures such as gamete intrafallopian transfer (GIFT). These devices include ovum aspiration needles used during transvaginal egg retrievals, embryo transfer catheters (tubes), GIFT catheters, and various insemination catheters.

ResCan Consultants, which maintains a data base of comparative costs on 200 000 medical devices from 800 companies, has no categories related to IVF. "These items would be a very small, esoteric market, so small we don't track it," noted ResCan's president.

Cook Canada Inc., a division of the Cook Group of Bloomington, Indiana, is one company that supplies this small, esoteric market. It estimates the total Canadian market for items specific to IVF and assisted conception at \$250 000. Cook Canada's sales volume in this area accounts for about 4 percent of its annual sales. "It's not big business," according to William Bobbie, a senior company representative.

Cook Canada sells about \$70 000 worth of ovum aspiration needles a year in Canada (at \$45 each), about 70 percent of the market. The company has a much smaller share of the market for catheters used in embryo transfer and AI (15 to 20 percent), largely because many users choose a much less expensive catheter, purchased from veterinary suppliers. Others import items from the United States. Cook Canada also makes customized tubes upon request.

Pharmascience Inc. of Montreal is another company that supplies medical devices to the NRT market. It initially became involved in this area when it distributed Serono drugs in Canada. But when Serono set up its own sales and marketing office here, Pharmascience decided to use its knowledge of this niche market to establish a diagnostic fertility division.

The division is just becoming established. It supplies products such as culture media for sperm and embryos, a "prep column" used in sperm preparation, an automated semen analysis system that is used mainly in research settings (very expensive, at \$20 000 to \$40 000), and other "bits and pieces." The division's director, V. Chebli, described the market as very diverse and speculated that nobody is making much money supplying it at the present time. "We have doctors begging us to get them this or that, though we make almost no money on it. It doesn't pay, but it's a service."

Conclusions

In Canada, the market for medical devices is estimated at \$2.5 billion annually. Included in this industry are manufacturers and distributors of products ranging from incontinence pads to laser surgery equipment. The subsectors with the most relevance to NRTs are diagnostic consumables (\$350 million total market, approximately \$7 million related to NRTs), ultrasound equipment (\$50 million or less, only a small percentage used in conjunction with NRTs), and custom items such as needles and catheters used in assisted reproduction and embryo transfer (estimated market \$250 000). Commercial laboratory testing is a related industry with an estimated \$700 million market nationwide (although NRTs account for only a small share of this total market, between 1 and 2 percent).

Diagnostics sales and commercial lab testing associated specifically with infertility assessment and assisted reproduction experienced substantial growth during the 1980s but have now levelled off, according to industry representatives. One reason commercial testing is thought to have plateaued is the fact that many infertility clinics have incorporated laboratory testing into clinic services. (In Ontario, there are concerns about the quality of laboratory testing done in private infertility clinics and doctors' offices, because medical practitioners are not required to participate in industry quality control programs.)

At \$250 000 annually, the market for specific devices used in conjunction with assisted conception is considered minuscule. Diagnostics sales related to infertility are more significant — approximately 2 percent of a \$350 million market, or \$7 million. For most diagnostics companies, fertility products represent only a small profit centre or may be offered to provide a complete line of laboratory testing products. The proportion of commercial lab testing associated with fertility assessment and assisted reproduction — approximately 2 percent of a \$700 million industry (\$14 million) — is substantial and possibly represents the least visible cost associated with NRTs.

Appendix 1. Sample Information Letters, Health Protection Branch

Information Letter

Health Protection Branch

August 15, 1988

Dear Doctor:

SUBJECT: Use of Protropin (Somatrem for injection) in Turner's Syndrome

This letter is to inform you that Protropin is no longer approved for use in the treatment of Turner's Syndrome. On June 3, 1988 a Notice of Compliance was issued to Genentech Canada approving Protropin for use in turner's Syndrome. Marketing approval was provided on the basis of evidence of increased short term growth in 4 to 12 year old girls, however no data were available for long term effects. Therefore, the company agreed to conduct long term studies,

Subsequently, the Health Protection Branch was made aware of the existence of additional information not submitted by Genentech Canada. On June 22, 1988 pursuant to a Branch request the company provided this information and advised that it was not in a position to conduct the long term studies which has formed part of the notice of Compliance.

Following discussions Genentech Canada requested the withdrawal of the indication for use of Protropin in the treatment of Turner's Syndrome and the Health Protection Branch agreed to the suspension of this claim.

A.J. Liston, Ph.D. Assistant Deputy Minister

Health and Welfare Canada

Health Protection Branch

714-X

Dear Doctor:

Please find enclosed a copy of the Health Protection Branch publication "Issues" concerning the unproven drug product 714-X, claimed as a cure for cancer or HIV infection.

The Branch wishes to emphasize that authorization to sell or distribute this product under the Emergency Drug Release program does not constitute approval of the product's safety of efficacy. 714-X is considered an unproven therapy; the Branch is not aware of any data to suggest promising activity of 714-X in animals or humans. Authorization to release this product to physicians is given on a patient-by-patient basis, for compassionate reasons.

Should you have questions relating to 714-X or the Emergency Drug Release Program, please contact the Bureau of Human Prescription Drugs at (613) 993-3105 between 08:30h and 16:30h Easter Standard Time. Written correspondence should be designated "Attention 714-X" and addressed to:

Gordon E. Johnson, Ph.D.
Director
Bureau of Human Prescription Drugs
Health and Welfare Canada
3rd Floor
Place Vanier, Tower "B"
355 River Road
Vanier, Ontario K1A 1B8

A.J. Liston, Ph.D. Assistant Deputy Minister

Health Protection Branch 1SSUES

714-X: AN UNPROVEN PRODUCT

The Health Protection Branch is concerned about recent public interest in the product 714-X, which is being claimed to be a cure for AIDS and cancer.

No scientific data has been provided to the Health Protection Branch to support these claims. Those reports which are available are anecdotal and circumstantial.

714-X is a chemical solution produced in Quebec by Gaston Naessens. It has been analyzed by the Health Protection Branch and found to contain a mixture of camphor, ammonium chloride and nitrate, sodium chloride, ethanol, and water.

At a recent meeting in Vancouver, the Expert Advisory Committee on HIV Therapy to the Health Protection Branch unanimously deplored the use of 714-X for the treatment of cancer and Human Immunodeficiency Virus (HIV) - related disease, including AIDS. The committee stressed that there could be secondary effects with this treatment.

Approval for the medical use of 714-X in Canada would require documentation of the safety and efficacy of this product. This requires that the manufacturer submit results of studies in animals and humans which provide substantial evidence to support the safety and efficacy of the drug for the claims indicated. Usually, this type of evidence is gathered over the course of many years through studies that are of an acceptable scientific nature approved by the Branch. The manufacturer would also be required to provide a detailed description of the manufacturing process.

Canadian Food and Drug Regulations provide for the use of an investigational drug in extenuating circumstances involving illness of a serious or life-threatening nature. Under the Emergency Drug Release Program (EDRP), a physician may request, on compassionate plea, a drug which has not been approved for either investigative human use (clinical trials) or for general marketing. In such as case, the Health Protection Branch may

authorize limited quantities of the drug to be released to that physician for a specific patient.

Most physicians are reluctant to administer a product for which there is no scientific evidence to indicate possible benefit, particularly if the product is associated with dramatic overstatement of anticipated benefit. It must be clearly understood that authorization under EDRP does not imply endorsement or approval in any way of the quality, the manufacturing process or the clinical use of the product.

It is merely an authority to the drug manufacturer to supply the product to the requesting physician, thereby ensuring that the product has been provided legally.

To date, no substantiative information regarding 714-X has been submitted to the Health Protection Branch. The Branch does not have any medical evidence to support the claims of usefulness of 714-X in the treatment of AIDS for cancer. Its safety is unproven.

At this time, the Health Protection Branch regards 714-X as an unproven product for which evidence to support treatment claims is lacking.

January 24, 1990

714-X: An unproven product is one of Health Protection Branch <u>Issues</u> produced by the Health Protection Branch of Health and Welfare Canada for the public, media and special interest groups concerned about health protection in Canada.

Appendix 2. PMAC Survey: Commercial Interests Involved in NRTs

About the Survey

The purpose of the attached survey is to gather information about the activities of pharmaceutical, biotechnical, diagnostic and medical devices companies, nationally and internationally, that are relevant to the mandate of the Royal Commission on New Reproductive Technologies.

The Commission is studying issues surrounding the use of new reproductive thechnologies (NRTs), including their ethical and legal implications. In addition, the terms of its mandate require the Commission

to examine the commercial aspects of these new technologies.

The technologies under review include *in vitro* fertilization, artificial insemination, prenatal diagnosis and genetic screening, gene therapy, embryo research and fetal tissue transplantation, among others (contraception and abortion are specifically excluded). The Commission is interested not only in technologies now in use, but also those undergoing research and development.

During public hearings last year, the Commission heard critical comment about the role of the pharmaceutical industry and other commercial interests involved in NRTs and how their agenda is driving NRTs. Much of the material presented was anecdotal in nature, based on

generalizations and perceptions.

Because there were few representations by the pharmaceutical industry during public hearings, the Commission believes there is a need to take a more detailed look at the role of commercial interests, including pharmaceutical companies, in providing and furthering NRTs.

To this end, the consulting firm Burson-Marsteller has been contracted by the Commission to research and write a "systems overview" paper on the commercial interests involved in NRTs, to be completed by the end of this year. As part of its work, Burson-Marsteller has prepared the attached survey which is being sent to PMAC member companies.

Some of the questions pertain to research and development activities of companies; in responding, companies should be as specific as they can be without jeopardizing corporate confidentiality.

The survey is divided into four sections:

- pharmaceutical products
- genetic testing/therapy
- diagnostics/devices/medical equipment
- other (STD test kits).

If parts of the survey would be more appropriately answered by an affiliated company or another division of your parent company, it is asked that the appropriate section be passed along to that company/division. The

consultants will rely on the parent pharmaceutical company to whom the survey was originally sent to coordinate the fully completed survey and return it to:

Burson-Marsteller

Health Services Group 80 Bloor Street West Toronto, Ontario M5S 2V1

Survey Questionnaire

As defined by the Royal Commission, new reproductive technologies (NRTs) include those products, practices and technologies connected to the treatment/prevention of infertility, assisted human conception, prenatal diagnosis, genetic testing/therapy and embryo/fetal tissue research. (The Commission's mandate specifically excludes contraception and abortion.)

Section A

Pharmaceutical Products

A.1. Does your company produce pharmaceutical products (prescription drugs) used in reproductive technologies such as in-vitro fertilization (IVF), artificial insemination or assisted conception, including drugs to stimulate follicle development and/or ovulation?

If so, please name the drug(s) and describe briefly their role in NRTs.

Note: Please include the following:

- drugs approved for other indications but which are being used investigationally in drug protocols for certain assisted conception techniques, e.g. IVF
- products which are being used investigationally or in clinical trials in Canada; and for which a Notice of Compliance application has been filed (indicate drug's status);
- products used to treat male infertility (except antibiotics);
- products used to treat endometriosis (except OCs).

Do not include:

- contraceptives;
- drugs used primarily to treat dysmenorrhea or symptoms of menopause;
- hormonal preparations used primarily for purposes other than achieving pregnancy

A.2.	Is your company engaged in research involving "fertility drugs" (such as those described above), or in the further development of such drugs, e.g. new formulations, delivery methods? Please describe briefly.
A.3.	Does research and development in the area of reproductive medicine (infertility treatment/assisted conception) represent a significant research and development thrust for your company? If yes, describe its significance.
A.4.	Do products used to treat infertility/assist conception represent a significant <u>potential market</u> for the pharmaceutical industry as a whole? Please comment and provide any quantitative information that you may have and wish to share.
A.5.	Do you have any comments/suggestions regarding what the role of government should be in regulating NRTs including IVF, artificial insemination, prenatal diagnosis, genetic testing/therapy, embryo research, fetal tissue transplantation?

A.6.	In your view, what effect would increased government regulation likely have on R&D investment in this area?
TO ((to fa	E OF PERSON(S) RESPONDING QUESTIONS IN SECTION A acilitate follow-up,
	cessary)
COM	IPANY NAME
ADD	RESS
TEL:	
ADD	ITIONAL COMMENTS:

Section B

Genetic Screening/Testing/Therapy

As defined by the Royal Commission, new reproductive technologies (NRTs) include those products, practices and technologies connected to the treatment/prevention of infertility, assisted human conception, prenatal diagnosis, genetic testing/therapy and embryo/fetal tissue research. (The Commission's mandate specifically excludes contraception and abortion.)

Note: The following questions may apply most appropriately to biotechnology, diagnostic or other divisions/affiliates of your company or parent company, nationally or internationally.

B.1. Does your company or any of its divisions/affiliates (biotechnical/diagnostic/other), nationally or internationally, currently market diagnostic kits/devices/other products used in genetic screening/

	200 Technologies 200
B.5. How would you des	cribe the commercial potential of such therapies?
NAME OF PERSON(S) ROTO QUESTIONS IN SECTION (to facilitate follow-up, as necessary)	
COMPANY NAME	
ADDRESS	
TEL:	
ADDITIONAL COMMENT	rs:
Section C	
Diagnostics/Devices/Me As defined by the F	dical Equipment Royal Commission, new reproductive technologies
(NRTs) include those pro treatment/prevention of diagnosis, genetic testing	ducts, practices and technologies connected to the f infertility, assisted human conception, prenatal g/therapy and embryo/fetal tissue research. (The specifically excludes contraception and abortion.)

Commorpial Involvement in New Pennsductive Technologie

Note: The following questions may apply most appropriately to diagnostic, medical equipment or other divisions/affiliates of your company or parent company, nationally or internationally.

C.1. Is your company or any of its divisions/affiliates, nationally or internationally, currently marketing or developing products/equipment/devices used in new reproductive technologies (as defined above), excluding those used in genetic screening/testing? Please describe briefly.

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C.2. In your opinion, is there a large current or potential market for such products/equipment/devices? How would you describe the current/potential market?
NAME OF PERSON(S) RESPONDING TO QUESTIONS IN SECTION C
(to facilitate follow-up, as necessary)
COMPANY NAME
ADDRESS
TEL:
ADDITIONAL COMMENTS:
Section D

Note: The following question may apply most appropriately to diagnostic, medical equipment or other divisions/affiliates of your company or parent company, nationally or

internationally.

Other

D.1.	produce tests/kits	or any of its divisions or affiliate companies used in doctors' offices to detect sexually s, e.g. kits to test for chlamydia?
TO S	IE OF PERSON(S) RE SECTION D (to facilita ecessary)	
COM	IPANY NAME	
ADD	RESS	
TEL:		
ADD	ITIONAL COMMENTS	5:

Appendix 3. PMAC Survey Results

Note: The questions below are paraphrased from the original. See sample survey (Appendix 2) for full text of questions.

QUESTION A.1.	Does your company produce pharmaceutical products used in reproductive technologies? (14 companies responded)
Company	Response
Allelix	no
Janssen	no
Miles	no
Sandoz	yes, Parlodel [®]

QUESTION A.1. (cont'd)	Does your company produce pharmaceutical products used in reproductive technologies? (14 companies responded)
Company	Response
Syntex	yes, Synarel [®] (for endometriosis)
Ciba-Geigy	no, but has hormone replacement for menopause
Roussel-Uclaf	no, but markets endometriosis drug in other countries
Riker	DTA
Wyeth-Ayerst Research	no
	Does your company produce pharmaceutical products used in reproductive technologies? (14 companies responded)
Sterling-Winthrop	yes, Danazol [®] (leading drug in endometriosis treatment)
Parke-Davis	no
Purdue Frederick	no
McNeil	DTA
Pharmacia	DTA
Astra	no
Akzo/Organon	yes, seeking HPB approval for 2 drugs/not on market yet
Glaxo	no

Is your company involved in research involving fertility drugs? (17 companies responded)
Response
yes, using recombinant DNA technology to produce fertility drugs such as FSH
no
no

QUESTION A.2. (cont'd)	Is your company involved in research involving fertility drugs? (17 companies responded)
Company	Response
Sandoz	evaluating non-ergot dopamine agonist for use in hyperprolactinaemia; evaluating cyclosporin A for suppression of rejection in fetal tissue transplant; evaluating long-acting Parlodel®
Syntex	peripherally yes (because of interest in endometriosis), but not a major R&D area; one trial in Canada using Synarel® in conjunction with IVF
Ciba-Geigy	no
Roussel-Uclaf	endocrinology research but not in area of reproduction
Riker	no
Wyeth-Ayerst Research	no
Sterling-Winthrop	yes, new delivery technology for Danazol®
Parke-Davis	no
Purdue Frederick	no
McNeil	no
Pharmacia	no
Astra	no
Akzo/Organon	yes, active research program directed toward fertility indications
Glaxo	no

QUESTION A.3.	Does R&D in the area of reproductive medicine represent a significant R&D thrust for your company? (16 companies responded)
Company	Response
Allelix	relatively modest
Janssen	no
Miles	· DTA
Sandoz	minor activity

QUESTION A.3. (cont'd)	Does R&D in the area of reproductive medicine represent a significant R&D thrust for your company? (16 companies responded)
Company	Response
Syntex	peripheral
Ciba-Geigy	no
Roussel-Uclaf	no
Riker	no
Wyeth-Ayerst Research	no
Sterling-Winthrop	no
Parke-Davis	no ·
Purdue Frederick	no
McNeil	no
Pharmacia	no
Astra	no
Akzo/Organon	yes, major portion of R&D budget
Glaxo	no .

QUESTION A.4.	Do products used to treat infertility/assist conception represent a significant market for the pharmaceutical industry as a whole? (14 companies responded)
Company	Response
Allelix	already a significant market (\$275 million worldwide); infertility is increasing; there is real commercial potential; biotechnology has a role to play
Janssen	little market potential
Miles	DTA
Sandoz	significant potential
Syntex	"minuscule" for the industry as a whole
Ciba-Geigy	moderate market but not trivial, "growing"

QUESTION A.5.	Do you have comments/suggestions regarding what the role of government should be in regulating NRTs? (15 companies responded)
Company	Response
Allelix	existing regulatory framework is adequate except as regards embryo research; should resist temptation to add another layer of costly regulation
Janssen	no
Miles	DTA
Sandoz	the current safety and efficacy evaluations should be supplemented by pharmacoeconomic considerations
Syntex	assisted conception requires regulation (standards of competency); who own embryos needs regulation; cannot stop progress in NRTs, can only regulate how used

QUESTION A.6.	In your view, what effect would increased government regulation likely have on R&D investment in this area? (9 companies responded)
Company	Response
Allelix	negative

QUESTION A.6. (cont'd)	In your view, what effect would increased government regulation likely have on R&D investment in this area? (9 companies responded)
Company	Response
Janssen	likely to be a disincentive
Miles	DTA
Sandoz	would affect time, complexity and cost of R&D must weigh benefit to target population versus gains due to decreased risk
Syntex	minimal effect for pharmaceutical industry as a whole
Ciba-Geigy	would increase cost and decrease investment
Roussel-Uclaf	there are problems with the different levels of government, i.e., feds approve but provinces fund
Riker	DTA
Wyeth-Ayerst Research	DTA
Sterling-Winthrop	increased regulation will decrease the attractiveness of Canada as a centre for R&D
Parke-Davis	DTA
Purdue Frederick	DTA
McNeil	government regulation usually decreases R&D investment
Pharmacia	DTA
Astra	DTA
Akzo/Organon	more government interference could translate into less R&D investment in this area
Glaxo	DTA

QUESTION B.1.	Does your company or any of its divisions/affiliates currently market products used in genetic testing or prenatal diagnosis? (13 companies responded)
Company	Response
Allelix	no
Janssen	no

QUESTION B.1.	Does your company or any of its divisions/affiliates currently market products used in genetic testing or prenatal diagnosis? (13 companies responded)
Company	Response
Miles	DTA
Sandoz	no
Syntex	no, but there's nothing new about this testing; it's already being done (amniocentesis); NRTs are only a refinement
Ciba-Geigy	no, are using biotechnology but not for genetic testing pursuits, rather for production of naturally occurring molecules (no hormones)
Roussel-Uclaf	does not believe so
Riker	no
Wyeth-Ayerst Research	no
Sterling-Winthrop	nc
Parke-Davis	DTA
Purdue Frederick	no
McNeil	no
Pharmacia	DTA
Astra	no
Akzo/Organon	DTA
Glaxo	no

QUESTION B.2.	Is your company or any of its divisions/affiliates engaged in R&D in the area of genetic testing or prenatal diagnosis? (14 companies responded)
Company	Response
Allelix	no
Janssen	no
Miles	DTA
Sandoz	no

QUESTION B.2.	Is your company or any of its divisions/affiliates engaged in R&D in the area of genetic testing or prenatal diagnosis? (14 companies responded)
Company	Response
Syntex	no, does R&D using genetic methods (molecular biology), but not in the area of reproduction
Ciba-Geigy	no, using biotechnology, but not for genetic screening or therapy
Roussel-Uclaf	no
Riker	no
Wyeth-Ayerst Research	no
Sterling-Winthrop	no
Parke-Davis	DTA
Purdue Frederick	no
McNeil	no
Pharmacia	no
Astra	no
Akzo/Organon	DTA
Glaxo	no

QUESTION B.3.	Is there a large potential market for genetic tests/screening methods? How would you describe the potential market? (12 companies responded)
Company	Response
Allelix	probably a large market but difficult to generate a return on investment; reimbursement issues will be important
Janssen	no idea
Miles	DTA
Sandoz	yes, multimillion dollar market
Syntex	a little more potential (than for fertility drugs)

QUESTION B.3. (cont'd)	Is there a large potential market for genetic tests/screening methods? How would you describe the potential market? (12 companies responded)
Company	Response
Ciba-Geigy	potentially market could be very large, but "touchy" because of ethical issues
Roussel-Uclaf	could be large, but statistically many genetic diseases are small in number (though very significant in nature)
Riker	DTA
Wyeth-Ayerst Research	rather limited
Sterling-Winthrop	yes, growing and needed
Parke-Davis	DTA
Purdue Frederick	no information available
McNeil	don't know
Pharmacia	no
Astra	not familiar with state of the art in prenatal diagnosis
Akzo/Organon	DTA
Glaxo	DTA

QUESTION B.4.	Is your company or any of its divisions/affiliates engaged in R&D in the area of genetic <i>therapy?</i> (13 companies responded)
Company	Response
Allelix	yes, applying molecular biology and recombinant DNA technology to identify, isolate, and sequence disease-causing genes
Janssen	no
Miles	DTA
Sandoz	no
Syntex	no
Ciba-Geigy	no
Roussel-Uclaf	no

QUESTION B.4.	Is your company or any of its divisions/affiliates engaged in R&D in the area of genetic <i>therapy?</i> (13 companies responded)
Company	Response
Riker	no
Wyeth-Ayerst Research	no
Sterling-Winthrop	yes, but very "immature"
Parke-Davis	DTA
Purdue Frederick	no
McNeil	no
Pharmacia	no
Astra	no
Akzo/Organon	DTA
Glaxo	DTA

QUESTION B.5.	How would you describe the commercial potential of genetic therapies? (6 companies responded)
Company	Response
Allelix	real but distant; first human trials of gene insertion technology have recently begun under strictly controlled conditions; the 1990s will see the commercialization of gene-therapy techniques for human disease, but their widespread use will not occur until after the year 2000
Janssen	no idea
Miles	DTA
Sandoz	very large potential
Syntex	DTA
Ciba-Geigy	DTA
Roussel-Uclaf	DTA
Riker	DTA
Wyeth-Ayerst Research	DTA

QUESTION B.5. (cont'd)	How would you describe the commercial potential of genetic therapies? (6 companies responded)					
Company	Response					
Sterling-Winthrop	too early to characterize					
Parke-Davis	DTA					
Purdue Frederick	DTA					
McNeil	don't know					
Pharmacia	DTA					
Astra	"mind-boggling," not just in commercial terms but moving the boundary between treatable and hitherto untreatable illness					
Akzo/Organon	DTA					
Glaxo	DTA					

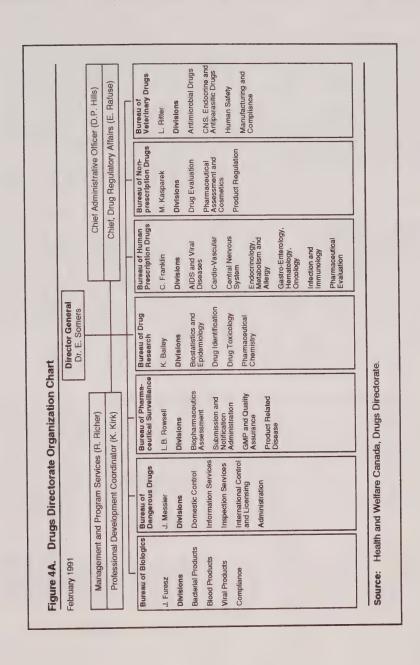
	ls your company or any of its divisions/affiliates					
QUESTION C.1.	developing or marketing equipment or devices used in NRTs? (12 companies responded)					
Company	Response					
Allelix	DTA					
Janssen	no					
Miles	DTA					
Sandoz	no					
Syntex	looking at ways to automate tests that already exist, e.g., hormone, endocrine tests					
Ciba-Geigy	no					
Roussel-Uclaf	yes, Hoechst is (diagnostics division)					
Riker	no					
Wyeth-Ayerst Research	no					
Sterling-Winthrop	no					
Parke-Davis	DTA					
Purdue Frederick	no					

QUESTION C.1.	Is your company or any of its divisions/affiliates developing or marketing equipment or devices used in NRTs? (12 companies responded)					
Company	Response					
McNeil	no					
Pharmacia	DTA					
Astra	no					
Akzo/Organon	DTA					
Glaxo	no					

QUESTION C.2.	Is your opinion, is there a large current or potential market for equipment/devices used in NRTs? (6 companies responded)
Company	Response
Allelix	DTA
Janssen	no idea
Miles	DTA
Sandoz	yes, large current market that will become larger over next 20 years
Syntex	DTA
Ciba-Geigy	DTA
Roussel-Uclaf	DTA
Riker	DTA
Wyeth-Ayerst Research	rather limited
Sterling-Winthrop	DTA
Parke-Davis	DTA
Purdue Frederick	DTA
McNeil	don't know
Pharmacia	don't know
Astra	no idea
Akzo/Organon	DTA
Glaxo	DTA

QUESTION D.1.	Does your company or any of its divisions/affiliates produce tests/kits used in doctors' offices to detect STDs? (10 companies responded)					
Company	Response					
Allelix	DTA					
Janssen	no					
Miles	DTA					
Sandoz	no					
Syntex	no					
Ciba-Geigy	DTA					
Roussel-Uclaf	DTA					
Riker	no					
Wyeth-Ayerst Research	no					
Sterling-Winthrop	no					
Parke-Davis	DTA					
Purdue Frederick	no					
McNeil	no					
Pharmacia	DTA					
Astra	no					
Akzo/Organon	DTA					
Glaxo	no					

Appendix 4. Drugs Directorate Organization Chart



Appendix 5. Examples of Methods Used in Genetic Testing

Indirect Tests

Maladaptive genes provide metabolic changes that can sometimes be measured to indicate the presence of incipient genetic disease. The substances measured may or may not be involved in causing the disease but are nevertheless associated with its presence.

Example: Phenylketonuria is a single-gene disease that causes mental retardation unless treatment with a special diet begins shortly after birth. The disease results from a genetic defect that prevents the breakdown of phenylalanine. As a consequence phenylalanine builds up in body fluids.

There are mass screening programs in place across Canada to detect disorders of phenylalanine metabolism in newborns. The screening test measures the level of phenylalanine in a blood sample taken from the newborn.

Gene Product Tests

The proteins derived from maladaptive genes can be measured directly to identify some diseases. The test must differentiate the abnormal form or activity of the protein from its usual form or activity.

Example: People with sickle cell anaemia possess an abnormal form of haemoglobin that causes red blood cells to change shape when the oxygen supply in the blood is below a certain point (e.g., during ordinary physical movement). The changed shape causes the cells to clump together, blocking blood vessels and interfering with circulation. The results can be fatal.

The abnormal blood cells produced by the sickle cell gene can be recognized by their abnormal sickle shape.

Chromosomal Analysis

Some genetic diseases involve very large alterations in the genetic material. Reliable techniques for examining chromosomes have been available for more than 30 years. Aberrations in number or structure (e.g., large insertions, deletions, or rearrangements) of chromosomes can be observed.

Example: Down syndrome is usually caused by the presence of an extra copy of chromosome 21. To reach a diagnosis, cells from an individual are treated so the chromosomes can be seen and distinguished from one another when magnified and photographed. This process is called karyotyping.

Recombinant DNA Technology

This technology can be used to establish the presence of, or potential for, disease involving genetic alterations as small as a change in one nucleotide. Recombinant DNA tests rely on the fact that a single strand of DNA will bind to another strand if it contains the complementary sequence of nucleotides.

(continued on next page)

Genetic Markers

The presence of, or susceptibility to, a genetic disease can be ascertained through use of genetic markers, even when the mutation causing the disease has not itself been identified. Markers are characteristic nucleotide sequences that are associated with, but are not necessarily the cause of, the disease or susceptibility. Example: Huntington disease is a neurological disorder whose symptoms begin in adulthood and include uncontrollable limb movements and mental deterioration. Diagnosis is now possible in some families before the symptoms of the disease appear. The risk of developing Huntington disease can be assessed by finding out whether a DNA sample from a person at risk for the disease binds to specific DNA strands containing the relevant genetic marker. A person with one parent affected by the disease has a 50 per cent chance of inheriting the disorder; currently available DNA testing may reduce the uncertainty over whether that person has inherited the disorder to 4 per cent.

Gene Probes

These work on the same principle as genetic markers but use strands of DNA that contain the actual sequence of the genetic mutation that causes the disease. Example: Haemophilia A results from an inability to make factor VIII, a protein involved in blood clotting. Several genetic mutations causing haemophilia A have been identified and diagnosis using gene probes is now possible.

Source: Science Council of Canada, *Genetics in Canadian Health Care*, Report 42 (Ottawa: The Council, 1991), 39-40.

Appendix 6. Mutant Genes and Genetic Markers

Examples of disorders for which mutant genes have been characterized:

Cystic fibrosis

Duchenne muscular dystrophy

Haemophilia A

Phenylketonuria

Premature coronary artery disease

Retinoblastoma

Sickle cell anaemia

Tay-Sachs disease

B-Thalassaemia

Von Willebrand disease

(continued on next page)

Examples of disorders for which genetic markers are available:

Adult-onset polycystic kidney disease

Familial Alzheimer's disease (in some families)

Fragile-X mental retardation

Huntington disease

Myotonic dystrophy

Neurofibromatosis

X-linked retinitis pigmentosa

Source: Science Council of Canada, Genetics in Canadian Health Care, Report

42 (Ottawa: The Council, 1991), 40.

Appendix 7. Neonatal Screening Programs by Province

Neonatal screening services are provided by the health ministries of the provinces and territories. Screening and follow-up for newborns in the Northwest Territories and Yukon is done in British Columbia, Alberta, Manitoba, and Quebec on the basis of proximity; the specific tests undertaken depend on which province does the screening. Participation in neonatal screening is voluntary; in all provinces and territories parents have an option to refuse.

	ВС	Alta	Sask	Man	Ont	Que	NB	NS	PEI	Nfld
Blood Tests										
Phenylketonuria		-								
Congenital hypothyroidism	=		•		•		-	•		٠
Aminocidopathies ¹		=				2				
Galactosaemia	-									
Congenital adrenal hyperplasia				H						
Biotinidase deficiency	■ p			m ^p						■ p
Duchenne muscular dystrophy				■ p						
Urine Tests										
Aminocidopathies (other than PKU)				3		■ 3				
						(c	ontin	ued c	n nex	t page

BC Alta Sask Man Ont Que NB NS PEI Nfld

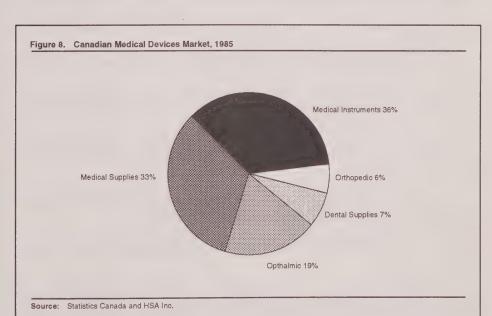
Neuroblastoma



- Alberta, Manitoba, and Newfoundland do general screening based on blood amino acid chromatography. Amino acid disorders that can be detected include maple syrup urine disease, tyrosinaemias, and hypermethionaemias.
- 2. Quebec has developed and offers a screening program for tyrosinaemia 1, because of the relatively high incidence of the disorder, particularly in the Chicoutimi region.
- 3. Screening for methylmalonic aciduria is available to parents in Quebec and Manitoba. Parents are asked to send dried urine samples on filter paper when the infant is two to three weeks of age. In Quebec, 94 per cent of families with newborns have chosen to participate; in Manitoba the figure is 85 per cent.
- p. pilot project

Source: Science Council of Canada, *Genetics in Canadian Health Care*, Report 42 (Ottawa: The Council, 1991), 104.

Appendix 8. Canadian Medical Devices Market



Appendix 9. Individuals and Organizations Contacted in the Preparation of This Report

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Bloom, Bradley. Marketing Manager, Inter Medico, Markham, Ontario.

Bobbie, William. General Manager, Cook Canada Inc., Stouffville, Ontario.

Booth, Marlene. Director, Regulatory Affairs, Serono Canada Inc., Mississauga, Ontario.

Bourgeault, Adele. Product Manager, Abbott Laboratories Limited, Montreal, Quebec.

Bowen, Elizabeth. Senior Industry Development Officer, Chemical and Bio-Industries Directorate, Industry, Science and Technology Canada, Ottawa, Ontario.

Buxton, Donald. President, Roussel Canada Ltd., Montreal, Canada.

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Carlisle, Dr. John. Deputy Registrar, College of Physicians and Surgeons of Ontario, Toronto, Ontario.

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Clay, Jill. Marketing Manager, Helix Biotech Corp., Richmond, British Columbia.

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Cournoyer, Marc. Manager, Communications and Internal Relations, Nordic Laboratories, Laval, Quebec.

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Going, Tony. Principal, Ernst and Young, Chartered Accountants, Ottawa, Ontario.

Goudey, John. Partner, Ernst and Young, Chartered Accountants, Toronto, Ontario.

Gould, Paul. Executive Director, Ontario Association of Medical Laboratories, Toronto, Ontario.

Gravelle, Ying. Author: Report on Survey to Review Private Sector Involvement in Genetic Disease-Related Biotechnology Development and Science Delivery; unpublished report for the Science Council of Canada, 1989.

Handelin, Dr. Barbara. Director of Molecular Genetics Diagnostics, Integrated Genetics Inc., Framingham, Massachusetts.

Hineson, Lee. Manager, Medical and Consumer Affairs, Serono Canada Inc., Mississauga, Ontario.

Ho, Dr. Isaac. Acting Section Head (Biotechnology), Patent Examination Branch, Department of Consumer and Corporate Affairs, Ottawa, Ontario.

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Johnson, Bruce. Product Manager, Merrill Dow Pharmaceuticals (Canada) Inc., Richmond Hill, Ontario.

Jones, Dr. Ken. Director of Drug Regulatory Affairs, Ciba-Geigy Canada Ltd., Mississauga, Ontario.

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Pharand, Robert. Acting Director, Fiscal Resources Branch, Ontario Ministry of Health, Toronto, Ontario.

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Shindler, Dr. David. Managing Director, Networks of Centres of Excellence, Canadian Genetic Diseases Network, Vancouver, British Columbia.

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Timmons, Paula. National Coordinator, Infertility Awareness Association of Canada, Ottawa, Ontario.

Walker, Dorothy. Acting Head, Operations Section, Bureau of Human Prescription Drugs, Drugs Directorate, Health Protection Branch, Health and Welfare Canada, Ottawa, Ontario.

Wise, Ted. President, Pharmascience Inc., Montreal, Quebec.

Worton, Dr. Ronald. Geneticist-in-Chief, Hospital for Sick Children, Toronto, Ontario; Board of Directors, American Society of Human Genetics; Associate Director, Canadian Genetic Diseases Network (Federal Centres of Excellence Program).

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The Role of the Biotechnology Industry in the Development of Clinical Diagnostic Materials for Prenatal Diagnosis

Gillian Chaloner-Larsson Fred Haynes Catherine Merritt



Executive Summary

Products for scientific and medical research and investigation are available commercially from many manufacturers around the world. These products fall into two categories: (1) materials for research use only, and (2) materials that have been approved by governmental regulatory authorities to be sold for diagnostic use. As technology advances, techniques once performed for research are developed and approved for diagnostic use. Products cannot be advertised or promoted for diagnostic use until approved.

This study describes the investigation of the extent and nature of industry involvement in the development, production, and promotion of products for the diagnosis of genetic disease prenatally. Inquiry was restricted to those methods of prenatal diagnosis (PND) using deoxyribonucleic acid (DNA) analysis. The study includes on-line surveys and listing of pertinent publications, journal and directory

This paper was completed for the Royal Commission on New Reproductive Technologies in April 1993.

studies, and the analysis of answers to questionnaires. The role of manufacturers of clinical diagnostic materials in the research, development, and promotion of agents used in prenatal diagnosis of

genetic disorders was examined.

Topics of particular interest were the relative roles of physicians/researchers and biotechnology manufacturers in developing diagnostic tests; manufacturers' perceptions of the markets, their interest in the clinical data, and their plans for the future; and identification of marketed materials and their uses. The latter included finding out to what extent laboratories were using commercial diagnostic kits, commercial research materials, or basic raw materials. Another line of inquiry was to determine sources of funding, and to assess if there was evidence of pressure by biotechnology companies on researchers and clinicians to develop and use tests. Research methods and sources are presented in context.

Analyses of questionnaires were performed to identify the current issues, including attitudes toward regulations, costs, and market goals (e.g., development of kits, sales to laboratories) of Canadian and U.S. manufacturers. The response rate was 20 percent for Canada and 33 percent for the United States. Materials found to be in use were those developed and sold for research use only. Market size was the major factor concerning decisions about entry to the market, followed by questions of competition and financing. The role of universal health care in Canada and government policies (seen by industry as restrictive) are discussed in relation to industry's motivation to expand.

Results offer a view of the current status of the literature, genetic diagnosis, and products. Recent work on PND using DNA methods is summarized by topic and type of technique or technology. Journal content is presented by topic and type of DNA probes and primers. Manufacturers and their products are listed for Canada and the United States.

At present, the market is small, and products being used by medical researchers in genetic disease are not yet approved "diagnostics." Industry appears to be waiting for the occurrence of further research and advances in genetics, which may provide a larger market for the development and introduction of diagnostic tests and kits. The role of the biotechnology industry may therefore change as knowledge grows and other applications become possible.

Introduction

This study was commissioned to survey the activities of the biotechnology industry in the development of diagnostic materials for prenatal diagnosis (PND). The study was restricted to the diagnostic technologies that involve deoxyribonucleic acid (DNA) methods of analysis.

The new DNA technologies have permitted researchers in biology and medicine to make analyses of minute amounts of DNA that can easily be extracted from small samples of cells, tissues, or blood. These

sophisticated techniques make it possible to examine genes at the molecular level. Mutant genes undergo changes in molecular structure, and many such mutations have been found to be the cause of several inherited diseases, for example, cystic fibrosis, muscular dystrophy, and haemophilia. As medical geneticists and researchers identify the genes and the mutations that cause genetic disease, these new DNA methods of analysis can be used to detect the mutations in the population by screening many people, or in specific cases by analyzing samples taken from the embryo.

Much of the equipment and many reagents necessary for sensitive and accurate DNA methods are already commercially available as research tools. As genes for inherited disease are discovered and sequenced, and the increased sensitivity of DNA tests makes PND feasible, the potential for biotechnology companies to develop commercial diagnostic test kits for these diseases can be realized. Such kits promoted for diagnostic purposes must be evaluated and approved by government.

Several avenues of approach were taken to uncover information on new developments in the industry.

The most recent literature was reviewed to identify the latest techniques of gene analysis, and for any reference to, authorship by, or support of that research by clinical diagnostic manufacturing companies.

Funding available to biotechnology companies, awarded either jointly with university or clinical researchers, or individually to companies by government programs for start-up biotechnology companies, was examined, as was funding by manufacturing companies to support research in PND. Information from genetic diagnostic laboratories in Canada was obtained to identify any commercial DNA-based diagnostic kits used in PND. Canadian biotechnology companies directly or indirectly supplying the prenatal diagnostic market were identified, and several were interviewed to discuss their perception of and their involvement in the prenatal diagnostic market. U.S. biotechnology companies marketing products for research and diagnosis of genetic disease were identified.

Selected Canadian and U.S. companies were contacted for information concerning their perception of the market potential for clinical diagnostic materials for prenatal use in Canada, and to ascertain their interest and efforts to gain entry to this market. In searching for pertinent data, the authors reviewed scientific and trade journals as well as conference proceedings for advertisements by biotechnology companies for prenatal diagnostic materials.

The key aim of this project was to provide a detailed account of the role of biotechnological manufacturers of clinical diagnostic materials in the research, development, and promotion of agents used in the prenatal diagnosis of genetic disorders.

Identification of the Materials Used in the Laboratory Techniques of PND

The first specific objective of the study was to identify the materials used in laboratory techniques for PND. Information on the methods and materials was obtained from publications on PND research and diagnosis, and from several genetic diagnostic laboratories in Canada.

Medical and biotechnology data bases, MEDLINE and BIOSIS, were searched for articles about PND that used DNA technologies. Key terms were "prenatal diagnosis" and "nucleic acid probes." Over 200 articles published from 1989 to 1992 were listed, and information available in the titles and abstracts of these articles was reviewed. (Table 1 lists the methods we identified as having been used for each disease reported.) The on-line searches were also used as a guide to relevant journals for more extensive review. The materials used for these PND techniques were obtained from the materials and methods section of selected articles, books, and texts.

Table 1. Results of the Data Base Search by Topic for Articles on PND Using DNA Methods*

Торіс	Number of articles	Techniques and technologies reported
Cystic fibrosis	28	linked probes, RFLP, PCR, direct gene diagnosis, direct gene probing, allelic association probes, DNA polymorphisms, rDNA, linkage equilibrium disequilibrium data
Duchenne's or Becker's muscular dystrophy	19	RFLP, Y-specific repeat segments, PCR, cDNA probes, oligoprimers, linkage analysis, cDNA deletion probes, deletion screening, Southern blot
Haemophilia A	15	RFLP, fetal sexing, PCR, probes, restriction enzyme analysis, Southern blot, rDNA linkage probes

Table 1. (cont'd)

Торіс	Number of articles	Techniques and technologies reported
Sexing	11	Y-specific probes, oligoprobes, fingerprinting, PCR, hybridization, molecular cytogenetics, DNA/DNA in situ hybridization
ß-thalassemia	10	synthetic oligoprobes, PCR, hybridization, restriction enzymes, dot blot, ASO, non- radioactive probes, linkage analysis
Fragile X syndrome	8	RFLP, DNA linkage, DNA probes for polymorphisms, rDNA techniques
Chromosome abnormalities	8	in situ hybridization, DA/DAPI probes, cloned DNA fragments
Polycystic kidney disease	8	RFLP, probes, restriction enzymes, DNA marker analysis, linked probes
Haemophilia B	7	RFLP, cloned specific probes, linked probes
Huntington's disease	7	DNA probes, linked DNA probes, screening probes
21-hydroxylase deficiency	6	cDNA probes, RFLP, Southern blot, HLA-linked DNA probes
Haemoglobinopathies	5	PCR, synthetic oligoanalysis, ASO probes, Southern blot, hybridization
Phenylketonuria	4	DNA probes, PCR, oligo- hybridization
Myotonic dystrophy	4	linked DNA probes, linkage analysis
Norrie's disease	3	DNA probes, deletion probes

Table 1. ((cont'd)
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Торіс	Number of articles	Techniques and technologies reported
X-linked chronic granulomatous disease	2	cDNA probes, RFLP, deletion analysis
Y-specific diseases	2	in situ hybridization, Y-specific probes, PCR, preimplantation analysis
Preimplantation PND	2	enzyme amplified trophoblast DNA, DNA probes, PCR
α ₁ -antitrypsin deficiency	1	PCR, ASO, RFLP
Down syndrome	1	**
DiGeorge syndrome	1	RFLP, DNA probes
Genetic gastrointestinal and liver disease	1	DNA probes
Familial amyloidotic polyneuropathy (FAP)	1	RFLP, PCR
Infantile neuronal ceroid lipofuscinosis	1	RFLP
Infantile hypophosphatasia	1	RFLP
Oculocerebrorenal syndrome	1	DNA linkage
Neonatal alloimmune thrombocytopenia	1	ASO probes
Pelizaeus-Merzbacher disease	1	RFLP
X-chromosome recessive ichthyosis	1	**
X-linked immunodeficiency	1	RFLP
Sexual aneuploidy	1	RFLP, linked probes

Table 1. (cont'd)

Topic	Number of articles	Techniques and technologies reported
General PND	22	rDNA, chorionic villus sampling, diagnostic DNA probes, dot blot, RFLP, PCR, DNA databanks, restriction enzymes

- * Articles were listed in MEDLINE and BIOSIS on-line searches, 1989 to 1992. Only titles and abstracts were listed. Data in table are from these two sources.
- ** Techniques not given in titles or abstracts.

Journals with five or more articles were chosen for further review to obtain specific information on materials and methods for PND using DNA techniques. Six journals — Prenatal Diagnosis, Clinical Genetics, Journal of Medical Genetics, American Journal of Medical Genetics, American Journal of Human Genetics, and Human Genetics — were found to be the most relevant. Issues published between January 1990 and March 1992 in the six journals and between March 1992 and March 1993 for three journals (Appendix 7) were reviewed for articles on DNA probes and primers used specifically for PND. Of the more than 100 probes and primers reported, only 8 were obtained from commercial or custom DNA service sources (Tables 2a and 2b) and none was a product sold for "diagnostic" use. All others were prepared in the research laboratory or obtained from research colleagues.

Table 2a. Manufacturers Identified in PND/DNA Literature, January 1990 to February/March 1992

Literature reviewed: 227 articles and 125 abstracts in 6 journals

References to manufacturer: 26

Industry authors: 14

Cetus Corporation 1 (retinoblastoma)
ICI Pharmaceuticals (United Kingdom) 2 (cystic fibrosis) (FAP)
DynCorp (United States) 1 (RFLP methods)
Integrated Genetics 2 (aneuploidy) (cystic fibrosis)
Integrated Genetics with Genzyme 1 (fetal cell isolation)

Table 2a. (cont'd)

Collaborative Research Inc. 1 (diabetes - not prenatal diagnosis)

Cellmark Diagnostics 2 (cystic fibrosis) (ARMS test)

Genescreen Inc. 1 (cystic fibrosis)

Pharmacia Diagnostica (Sweden) 1 (PCR methods)

Genetics and IVF Institute 1 (Kallmann's syndrome)

JCR Pharmaceuticals (Japan) 1 (muscular dystrophy)

Industry suppliers: 12

6 probes

Fresenius (Germany)

American Type Culture Collection (ATCC)

Synthecell

Imagenetics

Clontech (United States)

Regional DNA Synthesis Laboratory (Canada)

6 reagents: various

1 acknowledgment: Applied Biosystems

Table 2b. Manufacturers Identifed in PND/DNA Literature, March 1992 to February/March 1993

Literature reviewed: 69 articles and abstracts

Industry authors: 3

Cellmark 1

Integrated Genetics/Genzyme 1

Genetics and IVF Institute 1

Industry suppliers: 7

7 probes

2 Oswel DNA Service (Edinburgh) custom DNA synthesis

4 Oncor (chromosome probes)

1 ATCC

It is of interest to note that, of the 14 articles authored by biotechnology company researchers in the field of PND (4.0 percent of articles on PND/DNA), 10 were abstracts at the October 1991 8th International Congress of Human Genetics, and 3 were articles published in 1992, suggesting a recent involvement of biotechnology companies in research into DNA-based methods for PND. Of 69 articles and abstracts on

PND/DNA reviewed in three journals (Appendix 7) from March 1992 to February/March 1993, only 3 were authored by industry, giving a similar percentage of industry input in published research (4.3 percent).

Of the articles reviewed, 67 were Canadian reviews, directories, commentaries, or research publications (Table 3).

Table 3. Canadian Publications in PND/DNA			
1989 — March 1992 — February/March 1993			
Literature search: 352 articles and abstracts	Literature search: 69 articles and abstracts		
Canadian articles: 64	Canadian articles: not determined		
Disease-specific PND/DNA: 39	Canadian PND/DNA: 3		

Industry involvement: 0

Forty-two of these were articles on prenatal diagnosis of specific diseases, and only one had a reference to a biotechnology company or commercial biotechnology product. The article (Fraser et al. 1992) on haemophilia had custom DNA probes made at the Regional DNA Synthesis Laboratory at the University of Calgary.

Industry involvement: 1

Almost all of the commercial products used to analyze genes or DNA are enzymes, buffers, gel matrices, instruments, and various reagents that are not specific to PND. Only the specific short pieces of DNA used in DNA amplification (primers) and DNA probes used in DNA analysis are unique to the diagnosis of specific genetic diseases. All products identified in this study, including the PND-specific probes and primers, are research materials. These research products are the materials being used in medical genetics laboratories in hospitals and universities for research and diagnosis of genetic diseases.

Many advertisements appear for these research products in *Genetic Engineering News*, *Science*, and *Nature*, and several in *Biotech Products International*, but no advertisements for "diagnostic" products that were related to PND were found. Only two advertisements specifically identified genetic diseases. One, in *Nature*, for Genset (France) advertised oligoprimers for many different diseases (listed 36, including muscular dystrophy, cystic fibrosis, Huntington's disease, phenylketonuria (PKU), haemophilia, Tay-Sachs disease, and haemoglobinopathies), and two advertisements for BioProbe Systems (France) cystic fibrosis *F508 kit appeared in *Biotech Products International* and *Genetic Engineering News*.

These products were advertised for research purposes only. (The Genset probes are available in Canada through Bio/Can Scientific, Inc.)

Eight medical genetics laboratories were contacted to determine the type of products used for PND with DNA analysis. (See Appendix 2 for the questionnaire sent to each laboratory.) Six of the eight indicated that probes and primers were in use for PND in their laboratories as follows: inhouse preparation, 2; from research laboratories, 5; custom synthesis, 4; and commercial stock, 1. Two do not perform genetic analysis using DNA technology.

Most laboratories do not make their own probes and primers, but obtain them from other researchers, laboratories and/or commercial custom DNA service companies. Only one laboratory made all its own probes and primers. Another laboratory obtained probe(s) from the American Type Culture Collection (ATCC). The few commercial ready-made

probes and primers available for research are not used.

Of the 10 techniques performed in the laboratories for PND by DNA and related methods, all use commercial reagents such as enzymes, nucleotides, etc. Several laboratories used DNA amplification (two laboratories) and DNA sequencing (three laboratories) packages that supplied all the reagents, enzymes, and supplies needed for a defined number of tests. Most laboratories, however, indicated that they found these packages too expensive and made their own kits from basic reagents and enzymes. Other reagents used in these laboratories were for Southern blots, dot blots, messenger ribonucleic acid (mRNA) isolation, insert isolation, DNA labelling, and random priming. All of the commercial products used for these techniques in the eight laboratories studied are basic molecular biology reagents that are produced and distributed for research use.

The commercial research products listed by the laboratories were also identified in the literature and advertising searches. Two custom DNA synthesis companies, Dalton Chemicals and Regional Genetics (Alabama), used by two of the laboratories had not been identified in the company directories and surveys reviewed in the study.

Current Uses of DNA Materials for PND

The uses of these research materials for diagnosis were determined from a review of articles and abstracts published from January 1990 to March 1992. The specific product for PND by DNA techniques is the primer or probe constructed for the disease under study. Many hundreds of these are reported in the literature. Information published before December 1990 has been summarized in a data base of 2 687 published reports for over 300 different human conditions and disease states that can be detected directly or indirectly at the DNA level (Cooper and Schmidtke 1991). ATCC,

a Maryland company that is a commercial repository of biological materials, has numerous probes for genetic disease. A free on-line catalogue of the probes and primers is available from ATCC. A search of this data base for a few diseases listed revealed 24 probes for cystic fibrosis, 5 for haemophilia A, 6 for muscular dystrophy, and 1 for neurofibromatosis. ATCC had no probes or primers as of March 1992 for β -thalassemia, Huntington's disease, Tay-Sachs disease, fragile X syndrome, von Willebrand's disease, retinitis pigmentosa, myotonic dystrophy, PKU, or Down syndrome, indicating that researchers investigating these diseases at the genetic level have not deposited their DNA probes or primers with ATCC to be available to other researchers.

Techniques for the identification of gene mutations that result in disease include the analysis of DNA sequences, changes in specific sites for enzyme cleavage, changes in migration of specific DNA fragments in electrophoretic gels, and specific binding of known DNA sequences to complementary DNA in the gene (hybridization). Various methods of tagging the DNA with radioisotopes or with markers that can be visualized (colour reagents or ultraviolet) permit the detection of the DNA. These methods have been used for many years in molecular biology, but were initially not easily applicable to PND because large amounts of DNA were required for analysis. The materials used in DNA analysis include reagents, enzymes, gels, buffers, radioisotopes, visualization agents, media, and instruments for electrophoresis, sequencing, and temperature control.

In the late 1980s, a new technique, the polymerase chain reaction (PCR), was developed which produced an enzymatic amplification of very small amounts of DNA. This amplification technique uses specific pairs of short lengths of DNA, called primers. These are synthesized to match unique areas of DNA on either side of the DNA to be amplified. Under specific controlled conditions, the polymerase enzyme multiplies only the DNA between these primers. The PCR process depends on knowing sequences of the DNA in and around the gene to be amplified.

PCR made possible the analysis of very small amounts of DNA that can be isolated from the fetus. Using PCR, sophisticated techniques for DNA analysis have become techniques for PND. Medical geneticists can now analyze DNA taken from fetal cells (Shapiro et al. 1986; Jackson 1986; Rosenblatt et al. 1986; Orkin 1983; Fahy and Lippman 1988; Canadian Collaborative CVS-Amniocentesis Clinical Trial Group 1989; Klinger et al. 1991; Upadhyaya et al. 1990; Berhert et al. 1992), from preimplantation embryos (Muggleton-Harris 1990; Verlinsky et al. 1990a, 1990b; Varawalla et al. 1991; Lynch and Brown 1990; Griffin et al. 1991; Handyside et al. 1990; Monk 1991; Rechitsky et al. 1991; Simpson 1991; Grifo et al. 1991; Kontogianni et al. 1991; Strom et al. 1991; Arnheim et al. 1991; Handyside and Kontogianni 1991), and from fetal cells isolated from maternal blood (Bianchi et al. 1991; Mueller et al. 1990; Merel et al. 1991). Using primers flanking the DNA of interest, PCR can produce sufficient DNA of a specific gene for subsequent analysis. Alternatively, if a set of primers is designed

to match a segment of DNA in the gene that is suspected of having a mutation, the primer will not recognize the altered DNA and no amplification will take place. This PCR design permits direct detection of a mutation.

Where the gene site for a particular genetic disease is not known but its proximity to another gene has been established, DNA techniques for the detection of changes in this "linked" gene can provide clues to changes in the gene of interest. DNA techniques used in PND include many variations and adaptations of techniques to study a specific disease. The state of knowledge of the gene structure, the number, location, and type of mutations associated with each disease, and associated gene loci all affect the materials and methods used for diagnosing a specific disease. (Appendix 1 offers a detailed review of PCR and methods of DNA analysis used in PND.)

Manufacturers' Plans for Developing Diagnostics

Manufacturers' plans for the development of new clinical diagnostics for PND were investigated by reviewing biotechnology business journals, *BioScan*, and several other biotechnology directories (Table 4), as well as by requesting several companies to fill in a questionnaire (Appendices 3 and 4).

Table 4. Sources of Information Concerning Biotechnology Companies

Company Directory and Survey (Clinical Diagnostics & Biotechnology, Canada 1991)

Canadian Medical Device Directory (Canada, Industry, Science and Technology Canada, Chemical and Bio-Industries Directorate 1991)

Reference List of Health Science Research in Canada 1990-91 (Medical Research Council of Canada 1990)

Medical and Health Information Directory 1990, Vol. 1: Organizations, Agencies and Institutions (Kruzas et al. 1990)

Encyclopedia of Medical Organizations and Agencies (Kruzas et al. 1987)

BioScan (Worldwide Biotech Industry Reporting Service 1991)

The Biotechnology Directory 1992: Products, Companies, Research and Organizations (Coombs and Alston 1991)

1992 GEN Guide to Biotechnology Companies (Genetic Engineering News 1991)

Medical Technology Assessment Directory (Goodman 1988)

Biotechnology companies dealing with clinical diagnostics and DNA technologies are a smaller segment of the total biotechnology market. In 1991, a Canadian directory (Clinical Diagnostics & Biotechnology, Canada 1991) identified 129 companies in diagnostics and biotechnology.

Of the companies listed in the directory, only five indicated products specific to diagnosing inherited genetic diseases prenatally, or services for custom production of DNA probes and primers, and all of these market products for research use only. Therefore, in Canada, no biotechnology companies were identified that produced PND/DNA technology products that were promoted for diagnostic use. Table 5 summarizes the types of biotechnology and diagnostic companies in Canada.

Table 5. Diagnostic and Biotechnology Companies in Canada

Diagnostic and biotechnology companies in Canada	Number	PND
Clinical chemistry	66	
Cytology and histology	37	*
DNA probes or primers	28	5
Haematology	52	*
Home diagnostics	33	
Immunology	73	
Microbiology	73	
Non-isotopic immunoassay	55	*
Pregnancy kits	13	
Radioimmunoassay	43	*
Serology	52	
Tissue culture and animal sera	32	**
Urine/blood test strips	24	
Virology	55	

^{*} Some companies produce and/or distribute reagents or kits for cytological/biochemical/immunological tests that detect genetic abnormalities.

Source: Clinical Diagnostics & Biotechnology, Canada 1991.

Thirty-one biotechnology companies in Canada were selected to be contacted for further information. These companies were chosen because of their involvement in DNA technology or in the research or diagnosis of genetic disease. Two had gone out of business. The remaining 29 were contacted with a request to participate in the study by answering a series of questions about the PND market in Canada (see Appendix 3). Several

^{**} Cell culture is a preliminary procedure for some DNA tests.

companies were phoned to request an interview; three agreed. The rest were sent a letter with questions attached. A follow-up phone call was made to each company. Of the 29 companies contacted, 5 did not reply to the letters or phone calls, 6 were not interested in participating, 12 said they were not involved with the PND market, and 6 (20 percent) provided answers to the questions. The three companies interviewed were among these six.

The companies identified for contact that were not directly involved in PND are those supplying reagents and equipment for DNA analysis in general. They market their products to research laboratories that use molecular biological reagents, and do not target specific areas of research. Two of the companies unwilling to participate in this study advertise specific research products for inherited genetic diseases (cystic fibrosis, Duchenne's muscular dystrophy, and fragile X syndrome) in their catalogues. Their reason for declining to participate was because the questions were about diagnostics, and their products are for research.

The three companies that agreed to interviews were: a small Canadian biotechnology company that is a spinoff from a university hospital; a Canadian branch of a medium-sized U.S. biotechnology company that markets molecular biology reagents, supplies, and equipment for research; and a Canadian software company that markets an alpha-fetoprotein (AFP) screening analysis software program.

None of the six companies that responded deals directly with DNA diagnostic products, but they were willing to discuss the PND market in Canada. (Appendix 5 summarizes the responses.) The materials identified in the responses were all research materials. One company distributes a cystic fibrosis primer for research use, another distributes a fragile X probe kit for research use, and a third provides generic primers and restriction enzymes that are used in research into PND. Two companies provide custom DNA-synthesis services (preparation of DNA sequences to customers' specifications). (Although a commercial service, it does not involve the development and promotion of a specific product to the PND market.) One company, not in DNA technology, markets a software program for AFP screening. Two companies indicated an interest in developing probes in the future.

Screening for genetic disease and research were most often listed as the primary market for prenatal diagnostics. Reimbursement (by health insurance programs or companies) was most often given as the key issue before developing a PND market, with potential volume of use the next most important. Market size was ranked as the major factor in decisions about entry, followed by competition and financing.

The potential of the Canadian market was seen as small and fragmented. For example, the AFP software company that deals in diagnostics, not research materials (AFP kits are approved diagnostics), characterized the Canadian market as highly regulated for diagnostics (i.e., product approval, provincial licensing, reimbursement). The advantages of

universal health care were offset by disadvantages (as perceived by them) of poor funding for new tests, lack of money for technology transfer, multiple regulatory environments for diagnostics, slow entry to the market, and "conservative" health care policies. Two of the companies interviewed indicated that a Canadian company could not consider developing products for only the Canadian market and survive. Targeting the North American market was a must for the development of a diagnostic product. Approach by researchers to biotechnology companies was most often identified as the primary driver for developing new technologies.

As mentioned earlier, the number of companies that responded to the questions was small, but so is the number of companies involved in specific products for research and diagnosis of inherited genetic diseases. Many companies produce molecular biology products that are used for many applications, including PND. Many others produce cell media and chemicals or radioisotopes that are used in techniques that can be applied to PND. But none of the biotechnology or diagnostic companies contacted currently produces or distributes an approved diagnostic test specifically for PND. The companies that market disease-specific probes or primers, or that were aware that restriction enzymes, PCR materials, and many other reagents are used in diagnosis of genetic disease, emphasized that their products are promoted for research use only. Even the company with more than 50 percent of its products for prenatally determined genetic diseases (enzyme-based tests, not DNA) produces research products only.

The study identified Canadian companies and their activities related to PND/DNA (Table 6). The information was accumulated from directories, interviews, questionnaires, phone calls, and company catalogues. Five provide custom DNA synthesis services (for probes and primers), and only three have research products specific for the prenatal detection of genetic diseases. Information on companies in Canada that market products that are directly or indirectly related to PND/DNA is summarized in Table 6.

Company	PND and related product(s)
Bio/Can	restriction and DNA modifying enzymes, DNA purification products, thermal cyclers, blotting membranes Bio/Can distributed Genset primers for genetic disease (for research only)

Company	PND and related product(s)
	Bio/Can distributed Clontech DNA/PCR/sequencing research products, including cystic fibrosis and Duchenne's muscular dystrophy amplimers
Bio-Rad	Southern blotting apparatus, nucleic acid sequencing system, Zetaprobe blotting membranes, DNA purification kit
Boehringer Mannheim	wide range of reagents for DNA-based research
Cedarlane	Cedarlane distributed Oncor research products and equipment for nucleic acid analysis, research probes for 12 different chromosomes, and a fragile X probe and probe kit for research only
Dupont	reagents
FMG Integrated Biotechnical Laboratories Ltd.	gene cloning, probe development, gene probe reagents
Gelman	DNA-binding membranes, other reagents and equipment
Gibco BRL (Canadian Life Technologies Inc.)	research products (restriction enzymes, DN modifying enzymes, heat-stable DNA polymerase) and rapid cloning system for PCR products
HSC Research and Development LP	DNA probes, research biochemicals, substrates for genetic disease
New England Biolabs	restriction enzymes, heat-stable DNA polymerases, DNA modifying enzymes, DN, sequencing kit and reagents and equipment custom oligonucleotide synthesis
Pall Canada	immobilization membranes, DNA transfer materials
Pharmacia	reagents and equipment, custom oligonucleotide synthesis, automated sequencers, probe generation kits, sequencing kits, restriction enzymes, DNA modifying enzymes, heat-stable DNA polymerase, blotting membranes and equipment

Table 6. (c

Company	PND and related product(s)
Professional Diagnostics	custom antibodies for DNA chromosomes, DNA probes, fingerprinting, mapping
St. Joseph's Health Centre	non-isotopic DNA probes
Vetrogen	oligonucleotides, reagents, custom synthesis of probes Vetrogen distributed research probe for cystic fibrosis (made in France)
Sheldon Biotechnology Centre (McGill University)*	custom DNA and oligonucleotide synthesis
Regional DNA Synthesis Laboratory (University of Calgary)*	custom DNA and oligonucleotide synthesis

 Other universities may have associated companies for custom DNA synthesis.

Several biotechnology directories (*BioScan* 1991; Maryland (State) International Division 1990-1991; Coombs and Alston 1991; Genetic Engineering News 1991) were consulted to identify U.S. companies active in DNA research and analysis products, and genetic disease research and diagnostic materials. The *BioScan* directory provided the most comprehensive information on the activity of these companies and the status of their products and research and development. Companies were selected from listings under the DNA probe, genetic screening, gene cloning, and genetic analysis categories. Some information on U.S. biotechnology companies was also obtained from company catalogues and from Canadian companies that distribute U.S. company products. Table 7 lists the activities of companies selected from these categories that have direct or indirect involvement in PND.

Among the 26 companies, 12 provide DNA products specific to inherited genetic disease, 15 provide general or custom DNA products, and 4 provide laboratory diagnostic services. Several of these companies were contacted to request their response to questions about the market for PND in general and Canada's market. (If companies had Canadian subsidiaries or Canadian distributors, the Canadian company was contacted.)

U.S. biotechnology company	Research and development collaborations, commercial agreements (PND/total)	Products on market (PND/total)	Products in development (PND/total)	Comment
Abbott Labs	probe technology, ligase chain reaction (1/42)	(0)	(0)	not specific to PND
AMAC Inc.*	not available	DNA amplification, oligonucleotides, cystic fibrosis, Duchenne's muscular dystrophy or Becker's muscular dystrophy, PKU, others	not available	distributed for Genset (France) probes for research
Applied Biosystems Inc.	instruments/ reagents for DNA, computer DNA- base scanning (5/12)	(0)	not indicated	instruments only, not specific to PND
ATCC	characterization and preservation methods for cells, probes, etc. (not available)	many gene probes, cystic fibrosis, Duchenne's muscular dystrophy or Becker's muscular dystrophy, Haemophilia A, others	not indicated	repository and on-line searches
Biotrax Inc.	(0/2)	not indicated	test kits for human genetic disease (1/3)	not specific to PND

Table	e 7.	(cont'd)

U.S. biotechnology company	Research and development collaborations, commercial agreements (PND/total)	Products on market (PND/total)	Products in development (PND/total)	Comment
Cetus Corp.	PCR technology for disease diagnosis (2/36)	(3/13)	(2/25)	not specific to PND
Clontech Laboratories Inc.	not available	PCR primers for cystic fibrosis, Duchenne muscular dystrophy, custom probes and primers	not available	most research products not specific to PND
Collaborative Research Inc.	gene probes (5/16)	DNA probes, cystic fibrosis, polycystic kidney disease, chromosome abnormalities (3/5)	not indicated	diagnostic services reference laboratory
Enzo Biochem Inc.	DNA probes (includes prenatal defects) (1/20)	(0/11)	(0/4)	specific defects not indicated
Genetrix	diagnostics for human genetic disease	genetic testing services	not indicated	specific information not given
Genica Pharmaceuti- cals Corp.	Duchenne's muscular dystrophy/Becker's muscular dystrophy diagnostics, PCR DNA analysis, contract diagnostic research (2/8)	muscular dystrophy or	not indicated	reference testing laboratory
Gen-Probe Inc.	DNA diagnostics and DNA technologies (3/35)	(0/35)	(0/2)	not specific to PND

U.S. biotechnology company	Research and development collaborations, commercial agreements (PND/total)	Products on market (PND/total)	Products in development (PND/total)	Comment
Genzyme Corp.	fetal sampling technique (1/19)	PCR direct test for cystic fibrosis (1/11)	fetal cell separation, cystic fibrosis trans- membrane conductance regulator (CFTR) (2/6)	diagnosis and
ICI/Cellmark	DNA probes for cystic fibrosis (1/16)	(0/5)	not indicated	probe developed in United Kingdom
ImClone Systems Inc.	(0/9)	DNA probe amplification system	Repairchain reaction, DNA target amplification system	not specific to PND
Lifecodes Corp.	DNA hybridization diagnostics (2/15)	(0/9)	not indicated	sickle cell anaemia, unspecified birth defects
Molecular Analysis Inc.	in situ hybridization DNA/RNA probe technology (1/1)	trisomy screening kits (X,Y, 21,18,13) (1/3)	test kits for fetal sexing, muscular dystrophy, Down syndrome, Edward syndrome (1/1)	
Molecular Biosystems Inc.	oligonucleotides for diagnosis of genetic abnormalities (1/12)	(0/4)	(0/2)	abnormali- ties not specified

U.S. biotechnology company	Research and development collaborations, commercial agreements (PND/total)	market	Products in development (PND/total)	Comment
New England Biolabs Inc.	(0/2)	oligonucleotide, DNA enzyme research products	not indicated	not specific to PND
Nichols Institute	DNA probes, genetics, comprehensive laboratory testing services for hospitals (not indicated)	not indicated	not indicated	national reference laboratory for esoteric diagnosis
Oncor Inc.	(0/13)	instruments, probes, reagents, trisomy 21 kit, other chromosomes, fragile X probe kit (9/12)		exclusive worldwide licensing agreement for DNA probes wit University of Toronto
Promega Corp.	DNA enzymes and analysis systems (2/11)	(6/19)	not indicated	not specific to PND
Roche Holdings Ltd.	PCR technology licensing (2/35)	(0/21)	(0/22)	not specific to PND
Stratagene Cloning Systems	genetic diseases s	not indicated	not indicated	custom oligo- nucleotides and other DNA reagents
United States Biochemical Corp.	DNA enzymes and sequencing for research (2/2)	DNA reagents (7/15)	not indicated	research and production reagent

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U.S. biotechnology company	Research and development collaborations, commercial agreements (PND/total)	Products on market (PND/total)	Products in development (PND/total)	Comment
Vivigen Inc.**	not available	chromosome analysis, fragile X testing, DNA tests for cystic fibrosis and sickle cell anaemia	not available	diagnostic service laboratory and genetic repository

^{*} As of 1992 no longer distributes Genset primers.

Similar questions were asked of selected U.S. biotechnology companies to obtain their perception of the PND market in Canada. Twenty-six biotechnology companies in the United States were identified. Twenty-one were contacted by facsimile to request their participation in the study. The questions asked were a subset of the questions put to Canadian companies (Appendix 4). Follow-up phone calls were made to each company that did not respond to the facsimile. In total, 6 out of 21 companies responded. An additional company in a closely related field (fertility and pregnancy diagnostics) was interviewed. Of these seven responding companies, three indicated they were not in the PND field.

The number of U.S. companies that responded to the questions was small and they represent different areas of development: fertility and pregnancy diagnostics; a commercial diagnostic PND laboratory; a producer of reagents and diagnostics, including PND; a biotechnology company that both manufactures diagnostics and operates a diagnostic service laboratory for PND. (Appendix 6 summarizes their responses.)

Two companies market probes or primers for specific diseases: (a) cystic fibrosis, polycystic kidney disease, and fragile X syndrome; and (b) trisomies 21, 13, and 18, and X- and Y-chromosome disorders (research use). The primary market for use in the prenatal area was considered to be screening, with diagnosis second. The incidence of the target disease was mentioned most often as the key issue in developing a PND market, with potential volume of use and reimbursement levels second. Approach by researchers as well as active search by the company were considered to be the primary drivers for technologies for PND. Competition and market

^{**} Acquired by Genzyme Corporation in November 1992.

size, as was the case for the Canadian response, were the factors most commonly cited as influencing the decision to develop a technology and bring it to market. Canada's market was considered to be small, conservative, and too highly regulated. The advantages offered by the Canadian market were the lack of commercial genetic diagnostic laboratories and the existence of government research that needed to be marketed (i.e., not much competition). Disadvantages were the small size and, most often mentioned, the tight reimbursement policies.

The information obtained from manufacturers indicates that biotechnology companies in Canada are involved in developing research materials that can be used by medical geneticists for PND, but not in developing diagnostics. In the responses to the questions put to Canadian companies, only two indicated that they were interested in developing a market for probes for PND. One specified the probes would be for research, the other did not specify. These two companies were among the Canadian companies already in the PND market with research products for specific genetic diseases. One company that provides custom DNA primer synthesis services for genetic diseases indicated that it was not interested in developing products for diagnostics, preferring to continue to market research products only. This company has synthesized custom primers for PND-related genetic diseases for clients.

The situation in the United States is somewhat different. There are more biotechnology companies and funding possibilities, and a much larger market for PND. Many commercial diagnostic service laboratories for genetic testing have been established that offer services to physicians. The responses of the U.S. biotechnology companies seem to indicate that they consider the Canadian medical care system and the reimbursement policies in Canada to be restrictive.

Sources of Funding for Research into PND

Directories of funding organizations in Canada and the United States and reference lists of research grants awarded in Canada were reviewed to identify researchers active in the field of PND in Canada. Awards in Canada were from government agencies such as the Medical Research Council (MRC) or charitable foundations and associations (Medical Research Council of Canada 1990).

Several industry-associated grants may be awarded to researchers in Canada, such as the MRC Industry Grants and several other joint grants between MRC and specific industry sponsors (Medical Research Council of Canada 1990). During the time period studied, however, no research projects for PND were supported. In a comprehensive listing of health research grants in the United States, corporations active in commercial

health care that funded research were very limited, and none of the listed corporations funded projects related to PND (*Directory* 1992).

Officers at Industry, Science and Technology Canada (ISTC), the National Research Council (NRC) Biotechnology Contribution Fund, and NRC's Industry Research Assistance Program (IRAP) were contacted to obtain information about government financing of projects with commercial potential. These Canadian government programs have not been significantly involved in funding industry projects related to developing DNA technologies for PND. Only the IRAP has supported research during the last four years (four or five related projects concerning diagnosis of various disease states, DNA fingerprinting, and chromosome detection methods), but no project has succeeded in goals for commercialization (D. Cooper, personal communication). The names of companies that receive IRAP support are confidential and not publicly available unless the IRAP is acknowledged in publications or press releases.

In 1988 the Canadian government set up a series of Networks of Centres of Excellence (NCE) in various research fields. One of these is the Canadian Genetic Diseases Network, based at the University of British Columbia in Vancouver. The Canadian Genetic Diseases Network is a network of experts who study genetic disease. In A Report of the International Peer Review Committee, the Report of the Minister's Advisory Committee, and a NCE Backgrounder printed in an internal government publication, Innovaction, The Canadian Strategy for Science and Technology. in 1990, the Canadian Genetic Diseases Network was proposed as an integrated interdisciplinary approach to identify and analyze the structure and function of genes causing human diseases. The network was to have a commitment from industry and it was thought that such innovative research would result in major commercial opportunities for Canada in DNA diagnostics and therapeutics. The network had at that time 12 participating universities and research centres and a few industrial partners. MRC funds this group (Medical Research Council of Canada 1990), which, in turn, funds projects specific to genetic disease research. Reference to one PND research project so funded was included in MRC's list of funded research (Korneluk et al. 1991), but no information was available on the status of the network's participation in commercialization projects.

None of the Canadian companies that responded to the questionnaire had applied for or received funding from any of the government grants for industry. (In an April 1992 article, Zeidenberg reported a government announcement that increased funding was to be made available for technology transfer with private sector involvement. This may make this type of support more accessible to biotechnology manufacturers wishing to develop diagnostics.)

Investments by U.S. biotechnology companies in PND and related projects were assessed by reports in journals (*Biotech Products International, Nature, Science*), in biotechnology business publications (*MRC News* (UK), *Biotech Patent News*), and in biotechnology directories (Clinical

Diagnostics & Biotechnology, Canada, *BioScan*). Actual dollar amounts of financial investments were not obtainable. However, information available on the number and type of projects in research and development, products on the market, and products in development for the market was summarized (Table 7). Publicly available reports of joint ventures, buyouts, mergers, licensing, and other agreements indicate that the market is complex. Of the 26 U.S. companies reviewed (Table 7), and the 6 that responded to the questionnaire (Appendix 4), many were involved in PND/DNA-related projects and products, but there was no indication of products in clinical trials for approval by the U.S. Food and Drug Administration (FDA) as diagnostics for prenatal use.

At the "BioEast '92 Conference" in Washington, one company, Oncor, which produces research probes for chromosomes and fragile X syndrome, indicated plans to submit a fragile X kit for FDA approval (Oncor representative, personal communication). In April 1993, Oncor was contacted for information on the status of this product. It is still available only for research use. The *Biotech Patent News*, January 1992, "On the Horizon" page reported that Genzyme Corporation of Boston, Massachusetts, "has applied for a patent covering DNA encoding cystic fibrosis transmembrane regulator for use in treating and diagnosing cystic fibrosis" in the United States and Europe. There was no available information on the potential prenatal use of this product.

Manufacturers' Perceptions of Market Potential for Prenatal Diagnostics

The responses to the questions sent to Canadian biotechnology companies indicated that most companies identify screening and research as the potential markets for diagnostics for genetic disease. Screening would provide the volume of tests necessary for a commercially viable diagnostic product. U.S. companies identified screening as most important, and diagnostic testing as second in importance. These priorities reflect the fact that half of the responding U.S. companies operated commercial diagnostic service laboratories.

The Canadian companies that were interviewed indicated that the technologies did not lend themselves to kit format, and that the market was too small for companies to go through the process of getting government approvals for a diagnostic. Canadian companies generally thought that funding for development was inadequate and took too long to access. The company that markets AFP diagnostic software saw the different regulatory environments (federal, provincial) and the highly regulated licensing of diagnostic laboratories as detrimental to the marketing of diagnostics.

The U.S. companies' general impression of Canada's diagnostics market was that it was highly regulated under the medical care system,

was fragmented, and had tight reimbursement policies. It seems that there is a general agreement that the potential Canadian PND market is small and highly regulated.

Manufacturers' Interest in Clinical Data and Medical Research

Publications jointly reported by researchers in academia and industry were few. Tables 2a and 2b (review of articles in six journals from January 1990 to February/March 1993) and Table 3 (Canadian authors only from a computer search) list articles found in the literature concerning PND with industry involvement. Of the 296 articles from the journals, 14 had authors from industry; none of these originated in Canada. The computer search for Canadian authors from 1989 to 1993 found only one with an industry connection. All the articles were reports of research studies or new techniques. None was a report on clinical or animal studies of a potentially diagnostic product, nor was there a report of clinical studies in support of products being developed for approval as diagnostics.

In the *BioScan* directory (1991), current products in development were listed for each company, with information on products in clinical trials or under review for approval by the government. None of the companies listed a PND/DNA product that was involved in trials to gain approval as a diagnostic.

Most of the Canadian companies produce and/or distribute research reagents and instruments used in, but not specific to, PND/DNA methods. The companies interviewed were aware that DNA reagents and instruments and research products were used in medical genetics laboratories for diagnosis. They emphasized that their products were labelled, promoted, and sold for research only.

Medical Researchers Developing PND/DNA Products with Commercial Potential

From the search of the literature and conference proceedings concerning PND, the authors retrieved 42 publications by Canadians on specific diseases using prenatal DNA techniques (Table 3). Of these 42, 9 presented techniques with potential as diagnostic procedures. Four reported rapid detection methods for cystic fibrosis (Surh et al. 1991a; Rommens et al. 1990), neurofibromatosis (Ainsworth and Rodenhiser 1991), and β -thalassemia (Cai et al. 1991). One reported a non-isotopic method for *in situ* hybridization analysis of X and Y anomalies (Ray 1991). One dealt with strand separating gel electrophoresis detection of polymorphisms

in Duchenne's muscular dystrophy (Labuda et al. 1991), one with a specific DNA diagnostic probe for retinoblastoma (Goddard et al. 1990), one with rapid diagnosis of small muscular atrophy (MacKenzie et al. 1993), and the last reported a novel quantifiable method for detecting point mutations in haemophilia B (Cameron et al. 1991). None was co-authored by industry researchers.

Since about 1988, with the increase in biotechnological research with commercial potential and with the increase in university-based research with private sector partners, universities have set up technology transfer offices to help researchers with intellectual property rights, and to aid in the commercialization of the products of their research. In a BIONET newsletter (March 1992), contacts for the technology transfer offices were listed for 31 Canadian universities. Some of these technology transfer groups are independent companies, and several publish newsletters on the opportunities available, and report on successful project transfers. Six of these were contacted, but none was aware of any project related to PND that had been channelled through these particular offices.

No information was available from the Centre of Excellence for Genetic Diseases, which supports and promotes innovative research in the area of

prenatal diagnostics and therapeutics.

In the literature review conducted for this study, 14 articles concerning diagnosis of genetic disease were found to have authors from commercial manufacturers (not all of these applied directly to PND, but they had potential application). The manufacturers were Pharmacia Diagnostica (Sweden); Integrated Genetics, Cetus Corporation, Genetics and IVF Institute, Genescreen Inc., NTD Laboratories Inc., Genzyme, Collaborative Research Inc., DynCorp (United States); Cellmark Diagnostics, ICI Pharmaceuticals (United Kingdom); and JCR Pharmaceuticals (Japan). For 6 of the 14, all authors were from industry. The remaining eight were publications of collaborative research by industry, medical schools, research institutes, or universities. These reports were all publications or abstracts from October 1991 to March 1992.

Relative Roles of Physicians/Researchers and Biotechnology Manufacturers in Developing Diagnostic Tests

At the present time in Canada, prenatal diagnosis of genetic disease remains in the laboratories of medical geneticists at hospitals and universities. The state of the knowledge of inherited genetic diseases, the different methods of analysis for each disease, and the very small market related to each disease make commercial production of diagnostic tests in kit format non-viable at present, according to one company interviewed. Even for research use, very few "kits" have been marketed. One kit for

cystic fibrosis (for research only) made by BioProbe Systems in France and a fragile X probe kit for research use from Oncor in the United States are available. (Oncor's products are distributed in Canada by Cedarlane, Ontario.) Clontech (U.S.) markets pre-made primers for research for cystic fibrosis and Duchenne's muscular dystrophy, and Genset in France provides ready-made primers for many genetic diseases (both distributed in Canada by Bio/Can, Ontario) for research use.

The materials used for PND are the molecular biological reagents and instrumentation used for the various DNA amplification, sequencing and analysis procedures that are readily available from many commercial suppliers as research materials. Unique probes and primers are required for each disease, and often several are needed for detection of multiple mutations that occur in some diseases. At the present time in Canada, the input of biotechnology companies is minimal for prenatal diagnostics. Basic reagents and instruments, and a few research products (kits) from the United States and France are available. DNA-based prenatal techniques used in the Canadian laboratories that participated in this study do not currently make use of any of the disease-specific probe and primer kits available commercially. Almost all development and use of the products for diagnosis occur in the hospital and academic laboratories and involve medical geneticists. DNA research reagents and instruments are purchased, and primers and probes are custom made or obtained from other researchers.

In the United States and Canada, the promotion of a health care product is restricted to the approved use; therefore, manufacturers of research reagents may not promote these for use as diagnostics. However, physicians are not legally prevented from using drugs or diagnostics on their own patients in the practice of medicine. At the early stages of development of diagnostic techniques, medical researchers develop and use new methods in their efforts to provide health care. Diagnostics manufacturers become involved as techniques develop to the point where test formats and the market size make the investment potentially profitable. So far, the DNA techniques used for PND in Canada are still being performed and interpreted by medical researchers.

The larger prenatal diagnostic market in the United States has led to the appearance of commercial diagnostic service laboratories that perform DNA diagnostic tests. One article (Milunsky 1992) expresses concerns about these commercial laboratories and their capability to perform and interpret these diagnostic tests; the author anticipates problems as these companies promote their services to physicians who do not have medical genetics expertise.

The quality control and assurance on the performance of diagnostic tests is another concern voiced in the United States. At a conference, "Biotechnology and the Diagnosis of Genetic Disease" (Wilkinson and Perry 1991), several presentations focussed on the topic of control of quality of diagnostic test performance and interpretation. Regulations (Clinical

Laboratories Improvement Amendments) in the United States for *in vitro* diagnostics have tried to address this problem (United States, CLIA 1988). Regulations covering licensing, proficiency testing programs, and specific qualifications for personnel will be tightened for laboratories, and manufacturers may be subject to stricter controls on manufacturing, test instructions, and labelling.

Is There Pressure by Biotechnology Companies on Researchers and Clinicians to Develop PND/DNA?

Several publications in the 1980s indicated concern about the relationship between drug manufacturers and physicians (Lexchin 1988, 1989; Royal College of Physicians 1986). The implications in these publications were (a) that too many drugs were being dispensed by physicians on the basis of information, samples, and advertising materials provided by the manufacturers' sales representatives, and (b) that pharmaceutical manufacturers were "driving" the use of many products to protect their commercial investments. Although diagnostics were not discussed, such promotional techniques could apply only to diagnostic kits that are produced for physician office use. In Canada, provincial or private licensed laboratories carry out most routine diagnostic tests. These laboratories would be the target of any promotional efforts by diagnostics manufacturers, but at present in Canada these clinical laboratories do not perform PND/DNA tests.

Dangerous Diagnostics (Nelkin and Tancredi 1989, reviewed in Slack 1991 and Saxton 1990) discusses the danger that, once a diagnostic test is available, regardless of how valid the intended use, it could be misused by employers or insurance companies for inappropriate and potentially unethical drug or disease screening. It is relevant to know that drugs and medical devices, including diagnostics for treatment or diagnosis of human disease, are regulated by governments (the FDA in the United States and the Health Protection Branch of Health and Welfare in Canada). Prescription drugs and diagnostics must have submissions filed and receive approvals, or have notifications filed with the government, before sale to the public. The promotion of such materials is restricted and they can be advertised only to the medical profession (in scientific and biotechnology journals, by direct mail, by presentations, posters, and exhibition booths at conferences, and by sales representatives' visits to product users). Test kits and other products for research may not be promoted as diagnostics.

A search of several journals that publish research on PND, two general science journals, and several biotechnology and diagnostics journals was conducted to identify if there was advertising of products used in PND. Very little advertising was found in genetics journals: a total of 14 advertisements for commercial products and services in six genetics

journals over a 28-month publication period (Appendix 7). The biotechnology, diagnostics, and general science journals had large numbers of advertisements for DNA analysis products, instrumentation, and custom DNA synthesis services. All were for products to be used in research.

In the responses from manufacturers, no clear pattern emerged regarding the approaches used to market products. Journal advertising, exhibits, presentations, direct mail, and sales representative visits were important to some companies but not to others (Appendices 5 and 6). The small number of companies and their diverse interests do not permit a summary of this topic. Two companies indicated that telephone sales, press releases, and listing of their products in materials sections of scientific publications were important methods of selling their products.

There is no evidence from the information obtained in the present study that DNA products in biotechnology research are being promoted for PND purposes. The two Canadian companies interviewed emphasized that their products were promoted and sold for research use only. Examination of the advertisements and catalogues from these companies and others confirms this. All the products identified as materials for PND were products for research only. The responses to interviews and questionnaires indicated that companies are not generally interested in changing their focus at present. Without products approved or registered as diagnostics, these companies are restricted from approaching clinicians with their products. Biotechnology manufacturers will approach medical genetics laboratories in the ordinary course of their sales efforts since these laboratories require the research materials and instruments that these companies supply. Most of the Canadian laboratories that participated in this study prepare their own materials from basic reagents and obtain primers and probes from fellow researchers or have them custom made to their specifications. It does not seem, therefore, that the commercially available disease-specific research probes and primers for PND are being introduced to these laboratories by manufacturers.

Summary and Conclusions

The techniques used in the diagnosis of genetic disease are currently performed by experienced medical geneticists doing research or providing service in hospital and research laboratories.

The materials used are basic research materials and instruments, and unique probes and primers for specific disease detection. The latter are generally obtained from other researchers or are custom made.

PND assays are not available as diagnostic kits.

The Canadian market for PND is not large enough for a biotechnology manufacturer to consider developing a diagnostic product for a specific

disease. Entry to the PND market for a DNA diagnostic in Canada would be via the North American market.

The companies distributing research probes and primers for specific genetic diseases are not planning, at present, to develop these products for diagnostic use.

Three of six Canadian medical genetics laboratories consider PCR amplification and sequencing packages too expensive for routine use, so they purchase the individual reagents instead.

Reviews of Canadian research publications on PND indicate that several research teams have developed PND methods using DNA technologies that may have commercial potential.

None of the biotechnology companies that took part in the study has

applied for government support for prenatal diagnostic projects.

Canada's government funding programs for industry and biotechnology in health care have had very little activity in the prenatal diagnostic field. The IRAP has funded a few unsuccessful projects, and the Canadian Genetic Diseases Network has a mandate to promote the commercialization of promising Canadian research into diagnosis of genetic disease, including PND. No specific information on their present activities in PND was available. A 1992 report announced an increase in government funding for technology transfer projects in conjunction with the private sector.

A literature search and review of articles and abstracts on PND included only a small number of articles published by industry. From information in the articles it seems clear that, at present, prenatal diagnostic procedures using new DNA technologies are designed and developed by medical investigators, not by the diagnostics industry. Industry is only a minor source of published information on these techniques. Of 26 articles identified for 1990-92, 14 had authors from industry, and 12 identified suppliers of commercial research reagents (mostly equipment and supplies, and six probes) (Table 2a). From 1992 to 1993, a review of 69 articles from three journals identified three with authors from industry and seven probes that were from commercial or custom DNA sources and all sold for research use (Table 2b).

In the United States, the activity of the biotechnology industry pertaining to PND is in research materials and instruments, and in genetic diagnostic services laboratories. Only one company, Oncor, indicated that its product for the detection of fragile X syndrome would be submitted shortly for approval in the United States as an *in vitro* diagnostic under the medical device regulations. (As of April 1993, the Oncor fragile X probe was still available only as a research product.)

An April 1991 conference, "Biotechnology and the Diagnosis of Genetic Disease" (Wilkinson and Perry 1991), included several representatives from industry. Most were from commercial genetic diagnostic service laboratories. A representative from Enzo Biochem Inc., a company producing biotechnology products, provided the industry perspective:

With regard to genetic tests, the biotechnology industry can be said to be in a fairly fragmented state. It has not experienced the usual consolidation stage, and genetic diagnostic services are still being performed by small entrepreneurial companies and academic centers ... Industry is watching for the development of better test formats ... Diagnosis of genetic disease is in the correct hands now, i.e., the small labs, universities, and entrepreneurial start-up companies. These tests are new products, not nascent ones, but the major health care companies don't necessarily know how to market them. They will sit for a while at the starting line awaiting new developments.

In general, biotechnology companies are not actively pursuing government approval for genetic disease detection methods as diagnostics in PND. The situation is likely to change as the genetic defects become better known and the techniques become more defined and suitable for diagnostic kit format. The role of the biotechnology industry will also likely change as the technologies develop, as PND markets open up, as products become approved as diagnostics, and as the target of the industry's promotion efforts changes.

Appendix 1. Review of the Current Uses of DNA and Related Materials for PND

The general approach to PND using DNA is to isolate fetal DNA and, using a variety of molecular biological techniques, locate a mutation that predicts genetic disease. The fetal DNA may be extracted from amniotic fluid cells, chorionic villus cells, or trophoblast cells in maternal serum. For family linkage analysis using DNA, cells from blood, hair, or buccal cells of relatives may also be needed. The DNA used for analysis may be genomic, cloned DNA (i.e., genomic DNA that has been fragmented with restriction enzymes, incorporated into the genetic material of a "lambda" virus, and replicated many times in the bacterium Escherichia coli to produce large quantities of viral DNA containing specific human DNA segments [U.S. Office of Technology Assessment 1988]), or specific stretches of DNA that has been amplified by PCR. The DNA used for mutational detection is called a probe. It is tagged either by radiolabelling, fluorescent dyes, or biotinylated markers, and when complementary DNA (cDNA) sequences hybridize, the probe can be visualized. DNA is also used in PCR in the form of primers that are short stretches of oligonucleotides that bind with complementary flanking regions in the gene under study and serve as templates for the addition of more complementary nucleotides in a DNA chain spanning the gene. DNA primers are chosen from known sequences.

PCR

PCR permits the specific in vitro production of multiple copies of a defined fragment of DNA. This technique involves the primer-mediated enzymatic amplification of specific target sequences in genomic DNA by repeated cycles of (a) heat denaturation of the double-stranded template. (b) primer annealing, and (c) extension of the annealed primers with DNA polymerase. Target specificity is determined by the choice of short oligonucleotide primers that are designed to hybridize to opposite DNA strands flanking the sequence to be amplified. Successive cycles of amplification result in continuous doubling of, and exponential increase in, the sequence copy number as newly synthesized copies become available for primer binding (Reiss and Cooper 1990). The reaction is highly specific and extremely sensitive, enabling one copy of a sequence in a single cell to be detected (Lynch and Brown 1990). PCR is rapid: a typical 30-cycle amplification reaction takes approximately three hours. The method became widely established once Kogan et al. (1987) introduced the use of the thermostable Tag polymerase from Thermus aquaticus, which withstood the high temperatures needed for DNA denaturation, thereby allowing automation of the procedure. Because of patents obtained by the manufacturer of the enzyme, other companies are developing new thermostable polymerases from other organisms to overcome licensing obstacles.

PCR techniques allow the diagnosis of mutations both directly and indirectly. With appropriate primer selection, amplification products give confirmative results directly. PCR amplification products can also be cloned, sequenced, analyzed by restriction enzymes, blotted, etc., as for genomic DNA.

Direct Nucleotide Sequencing

Once DNA is isolated, a variety of techniques can be applied to detect mutation. Direct sequencing of the DNA will reveal mutations, especially in genomic DNA that has been amplified by PCR for a specific nucleotide sequence. Direct sequencing can also be performed on cloned genes, but is impractical for total genomic DNA.

Gel Electrophoresis

Alterations in nucleotide sequence can be detected by gel electrophoresis. The isolated DNA is digested with restriction enzymes, separated into different DNA fragments by agarose electrophoresis, and visualized as distinct bands by gel staining methods. A visual comparison of the location of the bands derived from parental DNA and from fetal DNA indicates whether a mutation in a site for a restriction enzyme (U.S. Office of Technology Assessment 1988) has been inherited.

Southern Blots

Once the test DNA has been isolated, cut by restriction enzymes, and separated by gel electrophoresis, visualization of the location of a particular segment of DNA is possible. The dissociated single-stranded DNA fragments are transferred to a nitrocellulose or nylon filter (Southern blot) and hybridized to a labelled cDNA probe. Again, alterations in banding patterns suggest a nucleotide substitution or deletion at a recognition site of one of the restriction enzymes.

Restriction Fragment Length Polymorphisms — "Marker" Identification

In many cases the DNA probes do not recognize the genetic locus itself, especially if it is characterized by a single base change. They hybridize to a closely linked site that includes a DNA polymorphism (marker) that alters the recognition site of a particular restriction enzyme. The failure of the restriction enzyme to cleave the DNA results in an alteration in the length of the DNA fragment that is recognized by the radiolabelled probe. Such restriction fragment length polymorphisms (RFLPs) (markers) have been of enormous value in PND, especially if the precise mutation is not known. However, they may be informative only in some families and DNA from relevant family members must be available in order to test for RFLPs.

Variable Number of Tandem Repeats

Variable number of tandem repeats (VNTR) loci represents a unique class of DNA polymorphisms. Unlike RFLPs, which detect the presence or absence of a restriction enzyme cleavage site, variation at VNTR loci is reflected in the number of times a particular DNA sequence is tandemly repeated. Such hypervariable loci have been found throughout the human genome and have also proven to be valuable genetic markers for human genome mapping and paternity testing because they are multiallelic, making most people heterozygous (Cahill et al. 1990).

Denaturing Gradient Gel Electrophoresis

Modifications of the standard electrophoretic procedure allow DNA to be separated not only on the basis of size, but also on the basis of sequence of nucleotides even if differences do not occur at restriction enzyme recognition sites. Double-stranded DNA dissociates into single-stranded DNA when it is heated or when it is exposed to denaturing chemicals. A gradient of increasing chemical strength can be produced in a gel so that every unique strand of DNA, travelling in the direction of the electric current, will not only separate by size but will begin to dissociate as it reaches its particular critical concentration of denaturing chemical where it stops migrating in the gel. A difference of only one nucleotide between

two otherwise identical strands of double-stranded DNA of 250 nucleotides in length is enough to cause the strands to dissociate at different concentrations of denaturing chemical (U.S. Office of Technology Assessment 1988). Again, a comparison of banding patterns between normal and test DNA using normal gel staining techniques (i.e., no radiolabelled probe) may identify mutations. This technique is called denaturing gradient gel electrophoresis or strand separating gel electrophoresis.

Single Strand Conformation Polymorphisms

Single strand conformation polymorphisms are detected by fractionating denatured, radiolabelled DNA on non-denaturing gels (Poduslo et al. 1991; Richards and Friend 1991).

Pulse Field Gel Electrophoresis

Pulse field gel electrophoresis allows the electrophoretic separation of very large DNA molecules of up to 10 megabases. This technique makes it possible to construct long-range physical maps, and to link up large regions of DNA (*MRC News* 1991). It is useful in detecting chromosome mutations that are intermediate in size between major rearrangements (observable by cytogenetic methods) and single base pair changes (U.S. Office of Technology Assessment 1988).

Dot Blot or Slot Blot Hybridization

In situations where the discrimination between normal and abnormal alleles relies on the failure of the probe to bind to one allele, electrophoresis is unnecessary and the analysis can be done by dot blots or slot blots rather than Southern blots.

Allele-Specific Oligonucleotides

Allele-specific oligonucleotide probes recognize point mutations and hybridize only to the normal or only to the abnormal allele (West 1989). These are used for mutation detection in Southern blot, dot blot or slot blot hybridizations.

Variations on PCR

As an alternative to allele-specific oligonucleotide probing, PCRs can be used as diagnostic systems. If oligonucleotide primers are synthesized to provide perfect matches with either normal or mutant alleles and the two primers mixed together with the DNA template, the preferentially bound template is extended from the 3' end and is detected on the agarose gel with normal staining techniques. This technique has been called competitive oligonucleotide priming (Gibbs et al. 1992) and amplification refractory mutation system (ARMS) (Newton et al. 1991).

Multiplex PCR involves the amplification of many sequences simultaneously, allowing screening of a number of deletion sites. This is particularly useful in a multiple deletion site disease such as Duchenne's

muscular dystrophy (Erlich 1992).

Recently it has been noted that the formation of heteroduplexes in PCR between normal and mutant sequences can be detected in both acrylamide (Rommens et al. 1990; Anglani 1990) and agarose gels (Shore and Myerowitz 1990), providing a convenient test for identification heterozygous individuals.

Inverted PCR is used for the analysis of DNA outside the boundaries of known sequence. A pair of primers is annealed to the known sequence but orientated in such a way that each primer extends in opposite directions across the regions of unknown sequence. By a series of manipulations the amplified flanking regions can be cloned and sequenced.

or sequenced directly (Lynch and Brown 1990; Erlich 1992).

Other amplification systems are also being developed. A thermostable DNA ligase has been developed that can be used in a temperature-cycled DNA amplification reaction to detect the presence of any defined sequence by the ligation of a pair of oligonucleotides that are adjacent when they are hybridized to a template DNA. Thermocycling between ligation and denaturation temperatures allows a geometric amplification to occur.

Amplification has been coupled with sequencing using thermostable reverse transcriptases from thermophilic bacteria in conjunction with a

ligase (Epicentre Technologies) or a polymerase (Amersham).

PCR has been coupled with the incorporation of a rare earth metal, chelate, which is visualized by time-resolved fluorescence. Different metal ions permit simultaneous analysis of allelic sequence variants in one reaction well of a microtitre plate. It also allows comparison with an internal control sequence.

In Situ Hybridization

In situ hybridization tests have been designed to allow prenatal identification of the major chromosomal aneuploidies using biotinylated or fluorescent DNA probes directly on interphase nuclei. chromosome-specific, non-centromeric DNA probe sets have been developed for chromosomes 21, 18, 13, X, and Y (Klinger et al. 1991).

Appendix 2. Laboratory Questionnaire

This sheet has been designed to elicit information on the use of commercial DNA products for direct/indirect (Commercial = from a manufacturer or repository: stock = premade; custom = made to customer specs) Please tick the boxes which apply to your lab and fill in the corresponding blanks detection of genetic disease.

	DNA/Oligonucleotide Probes or Primers	es or Prin	ners		
			From other	Commerc	Commercial product
Disease	Name/acronym of probe(s) or primer(s) (if available)	Prepared research in-house lab	research lab	source(s)	stock custom
Cystic fibrosis Muscular dystrophy Haemophilia A PKU Retinoblastoma Sickle cell anemia Tay-Sachs disease beta thalassemia Von Willebrand's disease Fragile X Huntington's disease Kragile X Chromosome abnormalities					

LAB $\overline{}$ (please indicate if lab may be identified in the study report (Y/N) $\overline{}$) initials of respondent:

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This sheet has been designed to elicit information about the availability, use, and source of commercial products and supplies for techniques used in the diagnosis of genetic disease.

(Basic = chemicals, buffers, enzymes, media, supplies) (Custom = specific order, made-to-purchasers' specs)

(Commercial = products sold for a specific use, complete package)

Please tick the boxes which apply to your lab operations and fill in the corresponding blanks

		Techniques	
		Specific com	mercial products
	Basic reagents	custom made manufacturer(s)	kits/packages manufacturer(s)
Fetal cell culture	0		
DNA amplification		0	0
Primer synthesis	Ö	0	0
In situ hybridization	o	0	
DNA sequencing		0	
Other			

LAB _	(please indicate if lab may be identified in the study report (Y/N)
initials	of respondent

COMMENTS

Appendix 3. Canadian Biotechnology Company Questionnaire

Your company has been identified through several directories and reports as a biotechnology company with an interest, or a potential interest, in the market for genetic disease diagnostics.

For a study on the present status of commercial *in vitro* diagnostics (IVD) for prenatal diagnosis (PND) of genetic disease in Canada, could you kindly answer the following questions.

Please indicate: (YD yes diagnostic use, YR yes research use, Y, N, NA, or comments as appropriate)

1:	Your company's present interest or involvement in genetic disease diagnostics is:
	a: production
	b: distribution
	c: production
	d: distribution
	e: production
	f: distribution
	g: interest in developing PND market for reagents \square probes \square
	biochemical tests 🗇 immunological tests 🗇
	h: other genetic disease diagnostics (e.g., forensics, paternity, cancer, infectious disease)
2:	If you answered yes to 1c or d
	a: probes are for what gene/disease(s)?

3:	What do you regard as the primary market areas for PND?
	a: screening
	c: research
	e: disease type
4:	What proportion of your diagnostic activities does PND represent?
	% of reagents% of diagnostics% of research prod
5:	What are the key issues in the development of the PND market?
	a: incidence of target disease b: severity of target disease c: clinical practice d: government regulations for IVDs
	e: availability of therapeutics f: reimbursement levels
6:	What are the factors involved in proceeding to develop a PND technology or bring it to market? (++ = major; + = medium; — = minor)
	Market Potential Other cont'd a: competition e: social need b: market size f: patentability c: entry to new market sector g: financing Other h: parent company policy d: development of new i: government approvals technology
7:	How do you evaluate the potential and nature of the Canadian market?
	a: size b: regulatory
	c: conservative d: other
8:	Do you have any relationships involving PND or other genetic diagnostics with Canadian:
	a: hospitals
	c: government labs
	e: physician-groups
	f: in the United States?

9:	What is your opinion of how new the primary driver	technologies f	or PND typi	cally develop? Is
	a: active search by company	3		
	b: approach by researchers	J		
	c: clinicians' suggestions	-		
	d: other			
10:	Does Canada have any advantag marketing of diagnostic materials			
11:	Have you participated in projects	on gen	etic disease	or PND funded by:
	a: IRAP			
	b: ISTC			0
	c: NRC Biotech			0
	d: Canadian Genetic Diseases	s Network		0
	e: MRC Industry Grant Progra	ım		O
	f: Provincial Program(s)			0
12:	Please rank these marketing approximately company for PND (1 being the marketing approximately company)			ance for your
	a: journal advertis			
	b: sales rep visits	0		
	c: direct mail			

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d: exhibits at conferences	
e: presentations	٥
f: other	

COMPANY $_$ (please indicate if the company may be identified in the summary of the responses (Y/N) $_$) initials of respondent $_$

COMMENTS OR ADDITIONAL INFORMATION

Appendix 4. U.S. Biotechnology Company Questionnaire

For a study on the present status of commercial *in vitro* diagnostics (IVD) for prenatal diagnosis (PND) of genetic disease in Canada, could you kindly answer the following questions.

(Please indicate: Y, N, NA, or comments as appropriate)

1:	Your company's present interest or involvement in genetic disease diagnostics is:
	research diagnostic
	a: production of reagents/supplies
	b: distribution 🗖 of reagents/supplies
	c: production of DNA probes or primers for PND
	d: distribution
	e: production
	f: distribution of biochemical/immunological PND tests
	h: other genetic disease diagnostics (e.g.: forensics, paternity, cancer)
2:	If you answered yes to 1c or d, probes/primers are for what diseases?
3:	What do you regard as the primary market areas for PND?
	a: screening b: diagnosis c: research
	d: research

4:	What proportion of your diagnostic activities does PND represent?
	% of reagents% of diagnostics% of research prod
5:	What are the key issues in the development of the PND market?
	a: incidence of target disease b: severity of target disease
	c: clinical practice d: government regulations for IVDs
	e: availability of therapeutics f: reimbursement levels
6:	What is your opinion of how new technologies for PND typically develop? Is the primary driver
	a: active search by company
	b: approach by researchers
	c: clinicians' suggestions
	d: other
7:	What are the factors involved in proceeding to develop a PND technology or bring it to market? (++ = major; + = medium; — = minor)
	Market Potential Other cont'd
	a: competition e: social need
	b: market size f: patentability
	c: entry to new market sector g: financing
	Other h: parent company policy
	d: development of new technology i: government approvals
8:	How do you evaluate the potential and nature of the Canadian market?
	a: size b: regulatory
	c: conservative d: other

	Do you have a Canadian:	ny relation	nships in	ovolving PND or other genetic o	diagnostics with
	a: hospitals	. 🗆	c: go	vernment labs 🔲 e: physic	ian-groups 🗖
	b: universit	ies 🗖	d: ted	ch-transfer programs 🗇	
	f: biotech o	ompanies			
			advanta	ges or disadvantages for the d	evelonment or
0: [r	Does Canada marketing of d	have any iagnostic i	materials	s for PND?	
1: F	marketing of d	iagnostic i	materials	proaches in order of importance	
1: F	marketing of d	ese marke	materials	proaches in order of importance	
1: F	Please rank th	iagnostic i	eting app	proaches in order of importance	e for your

COMPANY _ (please indicate if the company may be identified in the summary of the responses (Y/N) _) initials of respondent ____

COMMENTS

Appendix 5. Summary of Canadian Biotechnology **Company Responses**

The following summarizes the responses from the Canadian biotechnology companies. The summaries for the first two questions include responses from those companies that produce and distribute reagents for DNA.

1) Present involvement in genetic disease diagnosis (n = 10)

DNA reagents/supplies: production 6 (research only)

distribution 7 (research only)

production 2 (research only) DNA probes/primers:

distribution 4 (research only)

Biochemical/immunological

PND:

production 1 distribution 2

Other DNA diagnostics: forensics 4

> paternity 3 cancer 0

infectious disease 4

Interest in PND: reagents 3 probes/primers 2

biochem 2 immunology 3

computer analysis 1

2) Probe/primers (n = 6)

cystic fibrosis (research) 1 Diseases:

generic primers (research) 1

fragile X, chromosome probes (research) 1

restriction enzymes — Tay-Sachs (research) 1 restriction enzymes — fragile X (research) 1 [Non-probe:

AFP screening software 11

3) Primary market for PND (n = 6) (multiple answers given)

Screening 4

Research 4

Diagnosis 3

Clinical 2

4) Proportion of diagnostic activity = PND (n = 5)

preselection 1

3 companies: ≤5% (all research products) 1 company: 25% (AFP computer screening) 1 company: 50% (research products only)

5) Key issues in development of PND market (n = 6) (multiple answers)

incidence of target disease 3
severity of target disease 1
clinical practice 4
government regulations for diagnostics 2
availability of therapeutics 2
reimbursement levels 5
added by respondents:
funding levels 1
social perception of need 1
state of technology 1

Factors involved in developing and bringing a PND technology to market (n = 6)

T

- 7) Potential and nature of Canadian market (n = 5)
 - a. size: small, narrow.
 - b. regulatory: a problem; highly regulated because only certain labs are licensed (AFP diagnostics).
 - c. conservative: relatively conservative; more prochoice than the United States; less conservative than the United States, more than Europe; very conservative.
 - d. other: influence of societal issues; disadvantage of fragmented market.

8) Relationships with other institutions (n = 6, 4 yes, 2 no)

hospitals 3 universities 2 technology transfer programs 2 physician-groups 1 (AFP software) U.S. NIH grants 1 U.S. companies 1

9) Primary driver for PND technologies (n = 7)

active search by company 1
approach by researchers 4
clinicians' suggestions 2 (including AFP software)
other: availability of technology
availability of funding
physicians' knowledge of test procedures
popularity of a technology can affect market

10) Advantages/disadvantages to marketing in Canada (n = 5)

Advantages:

- appropriate health care sector infrastructure to implement programs
- universal health care, government decides costs, allocates scarce resources
- none

Disadvantages:

- no money for technology transfer
- slow entry to market
- no/poor funding
- many different regulatory environments
- conservative health care industry (physicians and hospitals), time delays on decisions
- Funding under following industrial grants (n = 6; 5 no, 1 yes)

IRAP 1 (not PND/DNA)
ISTC 0
NRC Biotech Initiatives 0
Canadian Genetic Diseases Network 0
MRC Industry Grants 0
Provincial programs 0

12)	Ranking	of marketing	and	promotional	approaches	(n = 6)
141	Namming	of mannethis	and	promonum	approactics	(11 - 0)

		•			(lowest)
approach	1	2	<u>3</u>	4	<u>5</u>
journal advertisements	0	1	1	2	2
sales representative visits	2	1	0	0	1
direct mail	1	2	1	1	0
conference exhibits	1	0	3	1	0
presentations	0	1	0	1	1
other:					
telephone sales		1			
press releases	1				
citation in scientific paper					

Appendix 6. Summary of U.S. Biotechnology Company Responses

U.S. biotechnology companies were contacted by facsimile to request their participation in the study. The questions asked (Appendix 4) were a subset of the questions put to Canadian companies (Appendix 3). The following summarizes the responses from the companies.

1) Present involvement in genetic disease diagnosis (n = 7)

DNA reagents/supplies: production 0 distribution 0

DNA probes/primers: production: research 1;

diagnostic 1

distribution: research 1;

diagnostic 2

Biochemical/immunological

PND:

production 0 distribution 0

Other DNA diagnostics:

forensics 2 paternity 3 cancer 2

infectious disease 1

Not involved: 3

2) Probe/primers (n = 4)

Diseases: cystic fibrosis, polycystic kidney disease, fragile

X: research plus diagnostic: 1 21, 13, 18 trisomies, X, Y: 1

not applicable: 2

3) Primary market for PND (n = 4) (multiple answers given)

Screening 4 Research 1 Diagnosis 3 Clinical 2

- 4) Proportion of diagnostic activity = PND (n = 4) not applicable; 30%; 75%; 90%
- 5) Key issues in development of PND market (n = 4) (multiple answers)

incidence of target disease 4
severity of target disease 1
clinical practice 3
government regulations for diagnostics 0
availability of therapeutics 1
reimbursement levels 3
added by respondents:
social need (will spur reimbursement) 1

6) Primary driver for PND technologies (n = 4)

active search by company 3 approach by researchers 3 clinicians' suggestions 1 other: social need 1

7) Factors involved in developing and bringing a PND technology to market (n = 4)

	major	medium	minor
competition	2	1	
market size	3		
new sector entry		1	1
development of new			
technology	1		1
social need	1	1	1
patentability	1		1
financing	1	1	1

parent company policy		1
government approvals	1	1

- 8) Potential and nature of Canadian market (n = 4)
 - a. size: very small, 10% U.S.; like California.
 - b. regulatory: too much paperwork; tight reimbursement.
 - c. conservative: conservative.
- 9) Relationships with Canadian institutions (n = 4)

none: 3

private commercial lab: 1

10) Advantages/disadvantages to marketing in Canada (n = 4)

Advantages:

- not aware of any advantages
- no single genetics diagnostic laboratories
- government funded research which needs to be marketed

Disadvantages:

- very small market
- very tight reimbursement
- understands Canada's reimbursement for new technologies difficult
- low population, loose distribution focus, difficult to keep sales representatives cost effective
- government reimbursement disadvantageous
- Ranking of marketing and promotional approaches (n = 4)

approach	1	2	<u>3</u>	4	(lowest) <u>5</u>
journal advertisements sales representative visits direct mail conference exhibits presentations	1 1 1 1	2 1 3	1	3	1

Appendix 7. Journals and Conference Proceedings Reviewed

Table 7A. Journals and Conference Proceedings Reviewed, January 1990-February/March 1992

- 1. Prenatal Diagnosis January 1990 to February 1992
 - a. 34/390 papers on PND using DNA techniques
 - b. Advertisements: industry 1; jobs 1; book 1
 - c. Industry support, authorship, or materials: 2
- 2. Clinical Genetics January 1990 to February 1992
 - a. 30/276 papers on PND using DNA techniques
 - b. Advertisements: jobs 1; courses 2
 - c. Industry support, authorship, or materials: 4
 - d. Abstracts from European Society of Human Genetics
 4 meetings, 28/475 abstracts on PND and DNA techniques
- 3. Journal of Medical Genetics January 1990 to February 1992
 - a. 64/400 papers on PND using DNA techniques
 - b. Advertisements: jobs 2; courses 1
 - c. Industry support, authorship, or materials: 5
 - d. Abstracts from meetings and articles on PND/DNA
 - i) Clinical Genetics Society (United Kingdom) 10/100
 - ii) Association of Clinical Cytogeneticists (United Kingdom) 3/18
 - Clinical Genetics Society and Clinical Molecular Genetics Society (United Kingdom) 18/73
 - iv) Clinical Genetics Society (United Kingdom) 10/27
- 4. American Journal of Medical Genetics January 1991 to March 1992
 - a. 22/458 papers on PND using DNA techniques
 - b. Advertisements: industry 2; jobs 2; book 1
 - c. Industry support, authorship, or materials: 3
 - d. Special issue on fragile X syndrome: Vol. 38 (2,3)
 23/75 papers on PND using DNA techniques
- 5. American Journal of Human Genetics January 1990 to March 1992
 - a. 40/825 papers on PND using DNA techniques
 - b. Advertisements: industry 12; jobs 7; fellowships 4
 - c. Industry support, authorship, or materials: 10
 - d. i) Special issue September 1990 (Suppl. 47) (3), Program
 Abstracts of the Annual Meeting of the American Society of
 Human Genetics: 5/84 abstracts in section on Prenatal and
 Perinatal Genetics

Table 7A. (cont'd)

- Special issue October 1991 (Suppl. 49) (4), 8th International Congress of Human Genetics — Proceedings, October 1991, Washington, D.C. Total presentations: 2 883. Session on Molecular Diagnosis 28/169 abstracts on PND/DNA. 19 corporate sponsors were from the biotechnology industry.
- 6. Human Genetics Vol. 84 (1) 1989 to Vol. 88 (4) 1992
 - a. 37/700 papers on PND using DNA techniques
 - b. Advertisements: industry 1
 - c. Industry support, authorship, or materials: 3
 - d. Vol. 85 (4) 1990: Special issue devoted to cystic fibrosis 38 papers, mostly screening populations, no PND

Other Journals

- 1. Journal of the Society of Obstetricians and Gynaecologists of Canada 1988-1991
 - a. no PND/DNA papers
 - b. no advertisements
- 2. Canadian Medical Association Journal 1990-91
 - a. no PND/DNA papers
 - b. no advertisements

Other Conferences and Symposia (no advertisements in any of the following)

- American Cytogenetics Technologists published in Cytogenetics and Cell Genetics 1991
 - a. Abstracts: none relevant to PND using DNA techniques, all cytogenetics
- 1989 Triennial Conference of the Institute of Medical Laboratory Sciences — published in *Medical Laboratory Sciences* Vol. 46 (Suppl. 1) 1989
 - a. 5/100 on prenatal diagnosis
- 3. 6th International Symposium on the Fetus as a Patient 1990 published in *Journal of Perinatal Medicine* Vol. 18 (Suppl. 1) 1990
 - a. no PND using DNA techniques
- 21st Annual Oak Ridge Conference on Advanced Analytical Concepts for the Clinical Laboratory — published in *Clinical Chemistry* 1989; topic was DNA technologies
 - a. no PND

Table 7A. (cont'd)

- Annual Meeting of the Society for the Study of Inborn Errors of Metabolism — published in *Journal of Inherited Metabolic Disease* Vol. 12 (Suppl. 2) 1989
 - a. 3/100 PND using DNA in 1989
- Annual Meeting of the Western Society for Pediatric Research
 1989 published in Clinical Research
 - a. none on PND
- 7. American Federation of Clinical Research 1990, 1991 conferences published in *Clinical Research*
 - a. 2/8 000 on PND using DNA techniques
- 8. 20th Albany Birth Defects Symposium 1989 published annually in Progress in Clinical and Biological Research; topic was fragile X cancer cytogenetics
 - a. 2/8 on PND using DNA techniques

Table 7B. Journals and Conference Proceedings Reviewed, March 1992-February/March 1993

- 1. Prenatal Diagnosis March 1992 to February 1993
 - a. 1/140 papers on PND using DNA techniques
 - b. Industry authorship: 1
 - c. Probes/primers (commercial or custom): 0
 - d. 44/182 abstracts on PND/DNA techniques 2 industry authors
 - 0 commercial or custom-made probes/primers
- 2. Clinical Genetics March 1992 to March 1993
 - a. 8/184 papers on PND using DNA techniques
 - b. Industry authorship: 0
 - c. Probes/primers (commercial or custom): 0
 - d. Abstracts: 0
- 3. Journal of Medical Genetics March 1992 to March 1993
 - a. 8/314 papers on PND using DNA techniques
 - b. Industry authorship: 0
 - c. Probes/primers (commercial or custom): 0
 - d. 1/78 and 7/69 abstracts
 - 0 industry authors
 - 0 commercial or custom-made probes/primers

Glossary of Acronyms

AFP alpha-fetoprotein

ARMS amplification refractory mutation system

ATCC American Type Culture Collection

cDNA complementary DNA
DA/DAPI fluorescent compound
DNA deoxyribonucleic acid

FDA Food and Drug Administration

IRAP Industry Research Assistance Program
ISTC Industry, Science and Technology Canada

MRC Medical Research Council

mRNA messenger RNA

NCE Networks of Centres of Excellence

NRC National Research Council PCR polymerase chain reaction

PKU phenylketonuria rDNA recombinant DNA

RFLP restriction fragment length polymorphism

RNA ribonucleic acid

VNTR variable number of tandem repeats

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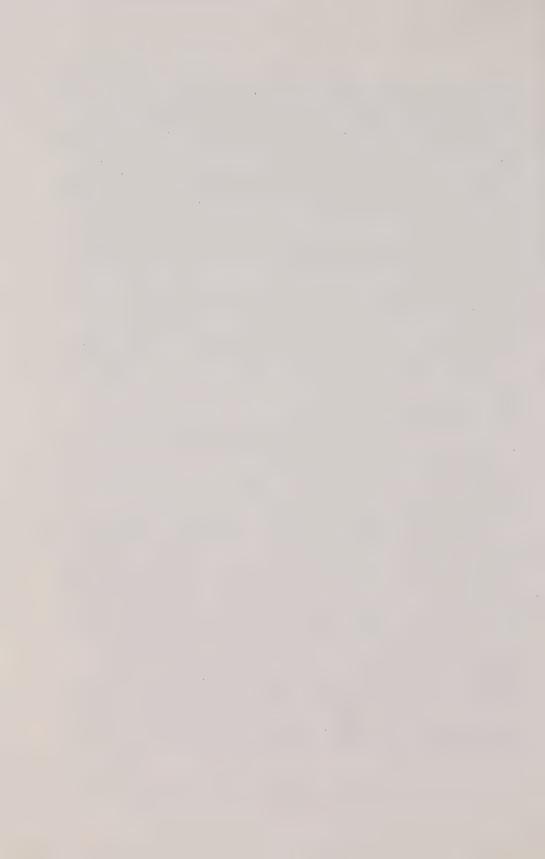
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Report on a Survey of Members of the Pharmaceutical Manufacturers Association of Canada and Biotechnology Companies

SPR Associates Inc.



Executive Summary

Members of the Pharmaceutical Manufacturers Association of Canada (PMAC) and a sample of Canadian biotechnology companies were surveyed to assess the use of human reproductive tissues in research and development. The surveys covered topics relating to sources and distribution of human reproductive tissues; research activities using human reproductive tissues; and policy, ethical, and commercial issues regarding reproductive technologies and human reproductive tissues. Human reproductive tissues were defined as ova, embryos, ovarian tissue, abortuses/fetal tissue, placentas, and sperm.

The survey included all 67 companies that are members of PMAC. The same questionnaire was sent to 26 biotechnology companies that were identified as potential users of human reproductive tissues. Written responses were received from 55 of the 67 PMAC members (82%) and from 20 of the 26 biotechnology companies surveyed (77%).

The surveys were generally successful in clarifying the scope of research involving human reproductive tissues being conducted by PMAC and biotechnology companies in Canada. There is a limited amount of research and development conducted in this country.

Although the overwhelming majority of PMAC respondents indicated that their companies conducted pharmaceutical research in both Canada and other countries, only one company reported any research using human reproductive tissues. This research is conducted outside of Canada. No distribution or redistribution of human reproductive tissues was reported.

Biotechnology respondents indicated a high level of general research activity in Canada (79%). Many of these respondents reported research in other countries — for example, the United States (42%), the United Kingdom (26%), and Germany (21%). A small percentage (11%)

were not conducting any research at all.

Some biotechnology companies (15%) indicated that research was being undertaken using human reproductive tissues. These research projects included the use of placentas and sperm, as well as the use of human cell lines originally derived from fetal lung fibroblast in the late 1950s and 1960s.

Introduction

As part of its mandate, the Royal Commission on New Reproductive Technologies was asked to examine commercial aspects of human reproductive tissues. The current survey was undertaken to document what the situation is in this country with regard to research using human reproductive tissues by pharmaceutical and biotechnology companies.

This survey of members of the Pharmaceutical Manufacturers Association of Canada (PMAC) and the biotechnology industry complemented the Commission's earlier survey of Canadian health care facilities offering obstetric, gynaecological, and pregnancy-termination services. The survey covered topics relating to sources and distribution of human reproductive tissues; research activities using human reproductive tissues; and policy, ethical, and commercial issues regarding reproductive technologies and human reproductive tissues.

This study of PMAC members' research and development activities and those of biotechnology companies using human reproductive tissues is important given the recent increase in interest in the use of human fetal tissues for treatment of disease. Diseases such as Parkinson's, DiGeorge's syndrome, diabetes, leukemia, and Alzheimer's have all been the subject of research using transplanted human fetal tissues. The list of current and potential experimental applications for human reproductive tissues continues to grow, so there may be a supply-and-demand imbalance in the future, as well as a range of social, ethical, and legal issues to be considered.¹

For example, cultured cell lines derived from human fetal tissues have been used for a number of decades by pharmaceutical and biotechnology companies in the development of vaccines such as the human polio vaccine. Fetal cell lines have also been used in the investigation of genetic manipulation and of viruses such as the human immunodeficiency virus (HIV).

Overview of the Survey Method

The Questionnaire

The survey questionnaire included a number of the same questions that were included in the survey of Canadian health care facilities offering obstetric, gynaecological, and pregnancy-termination services. It was designed to respect the need for confidentiality regarding trade secrets.

The PMAC survey included all 67 companies that are members of PMAC. Two covering letters were sent by Canada Post Special Letter to support the questionnaires; these were signed by the Commission Chairperson and the PMAC President. Both letters encouraged the companies to participate in the Commission surveys. Names and addresses of PMAC members were provided by the association.

The same questionnaire was also sent to 26 biotechnology companies. An initial list of names and addresses of biotechnology companies was supplied by the Commission. This list was then supplemented by SPR Associates after an investigation of reference sources (such as the Biotechnology Directory) revealed additional potential respondents.

Survey Procedures

Pretesting

A copy of the draft questionnaire and an accompanying letter explaining the purpose of the survey were distributed to a sample of 12 PMAC members identified as the appropriate people to whom the pretest questionnaire should be sent. They were asked to respond to the questionnaire and any lack of clarity or difficulties in completion of the questionnaire were assessed. A final questionnaire was produced after this process.

Survey Mailings

The survey package containing the questionnaire, a covering letter from the Chairperson of the Royal Commission on New Reproductive Technologies, and a letter supporting the survey from the PMAC President were mailed to PMAC by Canada Post Special Letter.

Hotline

A survey "help number" or "hotline" was provided for respondents who needed direction in completing the questionnaire, who sought assurances regarding confidentiality, or who had other queries about the study.

Reminders were sent to non-respondents by fax. Follow-up telephone calls were made where appropriate.

Response Rates

A number of companies indicated on returned questionnaires and in telephone follow-up that the survey did not apply to them as they do not undertake any research and development using human reproductive tissues. Altogether, written, fax, and telephone responses (including reports of inapplicability of the survey) were received from 55 of the 67 PMAC members (82%). A number of the PMAC companies indicated (by fax and letter) that the survey did not apply to them as they did not undertake any research involving human reproductive tissues. When these companies were contacted again by telephone, they generally confirmed that their non-response was because the firm did not see the survey as applying to its operations. No specific refusals to participate were obtained, but for 12 of the PMAC firms no representative could be contacted and no data were provided.

Responses were received from 20 of 26 biotechnology companies (77%).

Limitations of the Study

There is a limited amount of pharmaceutical research and development occurring in Canada. This context is important for the surveys. Throughout the course of the surveys, companies identified what they believe are obstacles existing in Canada for pharmaceutical companies wishing to conduct research. Multinational companies often therefore choose to locate their research and development companies in either Western Europe or the United States. This means that respondents from Canadian subsidiaries may not have complete information on the research activities of their affiliates in other countries. Thus, a complete picture of research and development using human reproductive tissues worldwide is not provided by this data. It was clear from returned surveys and follow-up phone calls that research in reproductive tissues may be going on worldwide, but it is not being done in Canada.

PMAC Survey Results

Distribution/Redistribution of Human Reproductive Tissues

Companies were asked whether they had distributed or redistributed any human reproductive tissues to other organizations or researchers for any purpose in the past year, including disposal. They were also asked to specify whether the end use of the tissues was for disposal, research, commercial use, or other uses, or was unknown.

Research Activities

Although the overwhelming majority of PMAC respondents indicated that their companies conduct research in both Canada and other countries (see Table 1), only one respondent reported research using reproductive tissues. That research study was conducted outside Canada using human reproductive tissues. That small research project (\$100 000 annual expenditures) is being conducted in collaboration with a non-profit body. It involves the use of sperm in research into immune contraception as an alternative to hormonal contraception.

Table 1. Countries in Which Research Is Conducted (n = 31 responding; responses are multiple and need not add to 100%)

n	%	
25	81	Canada
23	74	United States
20	65	United Kingdom
20	65	France
19	61	Germany
12	39	Sweden
12	39	Australia
13	42	other countries
4	13	no research conducted

Consistent with the lack of research projects using human reproductive tissues in Canada, PMAC respondents reported no other distribution or redistribution of human reproductive tissues from Canada to other countries.

Policy, Ethical, and Commercial Issues

Respondents were asked a series of questions regarding the policy, ethical, and commercial issues specific to reproductive technologies and human reproductive tissues. These included questions asking for:

- an assessment of the market potential for new products;
- estimates of the size of the market, in the next five years, for products developed through research;

- specific types of research likely to be undertaken by the industry in the next five years;
- potential benefits of the research;
- potential risks or problems;
- obstacles existing for companies in Canada wishing to conduct research in these areas:
- what policy changes (if any) would be desirable to encourage research and development in these areas;
- whether research and development in these areas was expanding more rapidly in countries other than in Canada;
- what moral, ethical issues face the industry in dealing with research in this area; and
- written procedures for ethical review of research involving human reproductive tissues.

Market Potential

Survey respondents were asked to assess the market potential for new products which require research using human reproductive tissues and/or products manufactured using human reproductive tissues. Most PMAC respondents said they were unable to respond to or comment on this question because this knowledge was outside their area of interest and experience. Among the few (22) respondents who did assess the market potential for new products requiring research or manufacturing using human reproductive tissues, opinions differed widely. Responses ranged from very low to very high market potential.

Table 2. Market Potential for New Products that Require Research Using Human Reproductive Tissues and/or Products Manufactured Using Human Reproductive Tissues (n = 22 responding)

n	%	Ratings	
7	32	1 low	
3	14	2 .	
5	23	3 .	
4	18	4 .	
3	14	5 high	

Companies varied in their estimates of the size of the market in Canada and worldwide for the next five years, with answers ranging from minimal to hundreds of millions of dollars. Overall, these respondents who provided estimates (12) felt that the market in Canada could be in the

millions or tens of millions of dollars, while the international market could more likely run in the tens of millions or hundreds of millions of dollars. Most (61), however, reported they were unable to estimate the potential dollar value of the market in the next five years.

Table 3. Estimate of the Size of the Market in the Next Five Years for Products Developed Through Research Using Human Reproductive Tissues and/or Products Manufactured Using Reproductive Tissues (n = 12 responding)

% 33 33	n 3	% 25	minimal
	3	25	minimal
22			
33	0	0	millions of dollars
33	3	25	tens of millions of dollars
0	4	33	hundreds of millions of dollars
1	2	17	cannot estimate at all
		0 4	0 4 33

Research Prospects

Respondents were asked to provide details on the types of research involving human reproductive tissues that would likely be undertaken in the next five years. In the opinion of respondents, this might include research related to fertility controls for both males and females, more effective infertility treatments, correction of genetic abnormalities, and treatments for Parkinson's disease.

Potential Benefits and Risks

When asked what potential benefits might be associated with this type of research, respondents replied that potential benefits would likely be safer and more effective treatments (e.g., for Parkinson's, leukemia, diabetes, and Alzheimer's), treatments that are more affordable and more accessible, and earlier identification of risks of disease.

The risks or problems associated with research using human reproductive tissues were identified as the expense of such research (including lack of tax incentives) and the restrictions on approvals imposed by the federal government and its regulatory bodies. Ethical and moral issues were also identified as areas of concern. The potential for public alienation or protests from special interest groups were also seen as possible problems.

Respondents answered a series of questions about the obstacles that may exist for companies in Canada wishing to conduct research in this area. Choices given ranged from federal government regulations and policies to provincial government policies, Canadian patent law, and other barriers. All these factors were identified as problems by PMAC members.

According to PMAC members, the expense of research and development of new products (including lack of tax incentives) is a significant factor affecting all pharmaceutical research in Canada, including that involving human reproductive tissues. Asked to identify moral/ethical issues in dealing with research using human reproductive tissues, respondents identified concern over public controversy and alienation as a powerful influence on pharmaceutical company operations, particularly where human reproductive tissues are involved. In the past, specific pharmaceutical products have been withdrawn from the market because of adverse publicity and public protests over a wide range of issues. A number of companies reported that these concerns limit their readiness to engage in research involving human reproductive tissues.

Respondents were generally in agreement that both federal and provincial government policies and regulations, coupled with the current Canadian patent law, have created obstacles for companies wishing to conduct research in Canada. For example, some pharmaceutical products that have general worldwide approval (including that of the FDA [Federal Drug Administration] in the United States) are still not approved in Canada after 10 years of submissions to the Health Protection Branch of Health and Welfare Canada. Pharmaceutical companies feel it has led to an overuse of the Emergency Drug Release Program.²

When they were asked what policy changes, if any, would be desirable to encourage research and development in these areas, PMAC members identified policy and regulation changes as essential for the growth of the industry and for research using human reproductive tissues. Respondents specifically mentioned the need for a reasonable reimbursement policy for innovation (e.g., a tax investment policy), adequate patent protection, official recognition of long-term benefits with the establishment of professional standards and safeguards, and the need for the Canadian drug regulatory review process to conform to world standards and to eliminate the problems associated with provincial variations.

Table 4. Obstacles for Companies in Canada that Wish to Conduct Research Using Human Reproductive Tissues (n = 12 responding; responses are multiple and need not add up to 100%)

n	%	
8	61	federal government regulations
1	8	Health Protection Branch approvals
5	42	federal government policies
3	25	provincial government policies
4	33	Canadian patent law
5	42	other barriers

The survey provided no assessments of the use of written protocols or procedures for ethical review of research involving human reproductive tissues, as these questions were asked only of those PMAC respondents reporting Canadian research with human reproductive tissue.

Results of the Survey of Biotechnology Companies

The same questions were asked of 26 biotechnology companies. The results are described below.

Research Activities Using Human Reproductive Tissues

Biotechnology companies form a small but rapidly growing industrial group in Canada. The sector deals with a wide range of problems, of which health applications are only a part (other applications include agriculture, forestry, and environment³).

Biotechnology company respondents indicated a high level (79%) of research activity in Canada. A small percentage (5%) were not conducting any research at all, while most respondents reported conducting research in countries other than Canada or in both Canada and other countries.

Table 5. Countries in Which Research Is Conducted (n = 19 responding; responses are multiple and need not add to 100%)

n	%	
15	79	Canada
8	42	United States
5	26	United Kingdom
1	5	France
4	21	Germany
2	11	Sweden
1	5	Australia
4	21	other countries
2	11	no research conducted

However, only three biotechnology companies (15%) responding to the survey indicated that research was being undertaken using human reproductive tissues. Research projects included the use of placentas and sperm, as well as the use of human cell lines originally derived from fetal lung fibroblast in the late 1950s and 1960s. These companies did not use written procedures, protocols, or guidelines for handling tissues used in research.

Of the biotechnology companies conducting research using human reproductive tissues, none reported obtaining tissues in Canada. Rather, these projects use sperm and placentas imported from other countries. (No explanation was given as to why these human reproductive tissues were imported.) SPR Associates identified Institut Mérieux in Lyon, France, as the primary source for worldwide distribution of products such as blood derivatives extracted from placental tissue. Institut Mérieux processes (from all sources worldwide) 15 tons of placentas per day.

A related study for the Commission showed that many of the 100 hospitals throughout Canada are among the regular sources of placentas for Institut Mérieux.

Policy, Ethical, and Commercial Issues

Market Potential

Most biotechnology companies indicated that they felt unable to comment on the market or commercial issues regarding reproductive technologies and human reproductive tissues, because those matters were outside their area of interest and experience. Among those respondents who did assess the market potential for new products (eight companies) requiring research and/or manufacturing using human reproductive tissues, opinions varied. Four companies indicated a high market potential for products, two predicted a low market potential, and two predicted neither a high nor a low potential.⁴

Table 6. Market Potential for New Products that Require Research Using Human Reproductive Tissues and/or Products Manufactured Using Human Reproductive Tissues (n = 8 responding)

n	Ratings
2	1 low
0	2 .
2	3 .
3	4 .
1	5 high

Four companies estimated the potential market in Canada to be minimal, while two estimated it to be in the tens of millions of dollars. The potential international market was estimated to be minimal by two companies; millions of dollars by two; and hundreds of millions of dollars by two (see Table 7). Two of those answering these questions indicated they "could not estimate" the potential market size.

Table 7. Estimate of the Size of the Market in the Next Five Years for Products Developed Through Research Using Human Reproductive Tissues and/or Products Manufactured Using Human Reproductive Tissues (n = 8 responding)

Canada	Internationally	
n	n	
4	2	minimal
0	2	millions of dollars
2	0	tens of millions of dollars
0	2	hundreds of millions of dollars
2	2	could not estimate

Research Prospects

When asked about the type of research that would likely occur in the next five years, companies provided a range of answers. Some identified cancer diagnostics and research on human placentas, including the purification of proteins and possible treatments for human infertility, as specific types of research involving human reproductive tissues that are likely to be undertaken by the biotechnology industry in the next five years.

Potential Benefits and Risks

In the view of biotechnology respondents, the primary potential benefit of research using human reproductive tissues is likely to be the development of diagnostic materials.

Obstacles for Companies

The difficulty in obtaining human reproductive tissues was seen as a major obstacle for biotechnology companies wishing to conduct research in Canada. A number of biotechnology respondents noted access to tissues as a problem. Others (similar to responses for PMAC companies surveyed) reported that federal government regulations presented obstacles.

Easier access to human reproductive tissues was mentioned frequently as a key change that would encourage biotechnology companies to conduct research and development in this area.

Summary

The survey findings suggest that use of human reproductive tissues in research conducted by Canadian pharmaceutical and biotechnology companies is minimal. The only use documented in Canada was of sperm and placentas. A variety of obstacles to doing research in this field were identified by companies. Institut Mérieux in France provides a striking illustration of a firm establishing an important niche in the field of human reproductive research.

Within the limitations of this survey, it is clear that pharmaceutical and biotechnology companies regard government action on tax incentives and restrictions on approvals and access to human reproductive tissues, in addition to clear directions with respect to ethical issues, as ways of promoting the growth of research in Canada.

Appendix 1. Survey Questionnaire

Survey of the Pharmaceutical Manufacturers of Canada and a sample of Canadian Biotechnology Companies Regarding Research, Use, and Distribution of Human Reproductive Tissues

INTRODUCTION AND INSTRUCTIONS: In accordance with its mandate, the Royal Commission on New Reproductive Technologies requires information regarding a variety of topics dealing with the use/distribution of human reproductive tissues.

This survey of biotechnology companies is an important part of this work. The survey complements a previous survey by Dr. Alan Fine of Dalhousie University, Faculty of Medicine, and a survey conducted for the Commission of Canadian health care facilities offering obstetric and gynecological services.

Your response to the new survey is needed regardless of whether or not your organization deals with human reproductive tissues in any way.

Please be assured that the information you provide will remain strictly confidential. Only aggregated data will be published. Institutions, agencies, or researchers identified by you as sources and/or recipients of tissues will not be revealed in any way. Questions will not require disclosure of proprietary information. Furthermore, all questionnaires will be destroyed by the company conducting the survey for the Commission at the conclusion of the research.

Most of the following questions require only a check mark or a brief written answer. In some places, depending on your specific answer, you are asked to skip to another question further on. Please follow these instructions. Where text answers are requested, please type or print using ink. In some cases, we ask you to attach copies of documents (e.g., protocols/consent forms). Please be sure to attach these documents even if you have provided them already to the Commission in connection with other projects/surveys. Be sure to read each question carefully to determine how the question applies to your organization. For any questions that you think would require disclosure of proprietary information, please answer "cannot be disclosed; proprietary answer is strictly confidential."

Please return the survey within the next week by fax to: (416) 467-0517, or by mail to:

Survey of Biotechnology Companies Royal Commission on New Reproductive Technologies 2318 Danforth Avenue, 2nd Floor Toronto, Ontario M4C 1K7

If you have any questions, please telephone the survey "hotline" at (416) 467-8430.

Thank you in advance for your time and assistance.

A. Research Activities Using Human Reproductive Tissues

1. In which countries does your company (including parent company or other non-Canadian affiliates or subsidiaries) conduct research? The phrase "conduct research" includes research conducted indirectly (e.g., purchased from or contracted with other organizations/individuals, or funded by grants to medical laboratories, foundations, or universities). (CHECK ALL THAT APPLY)

Canada
United States
United Kingdom
France
Germany
Sweden
Australia
Other countries (PLEASE SPECIFY):
None of the above ---> (GO TO SECTION D, QUESTION 7)

2.(a) Does your company (including parent company/affiliates) conduct any research using human reproductive tissues?

(Human reproductive tissues include: ova, embryos, ovarian tissue, abortuses/fetal tissue, placentas, sperm.)

Yes

No ---> (ALL RESPONDENTS ANSWERING "NO" SHOULD GO TO SECTION D, QUESTION 7)

NOTE: COMPLETION OF QUESTIONS 7 TO 16 IS NEEDED, REGARDLESS OF WHETHER OR NOT YOUR COMPANY OR AFFILIATES CONDUCT ANY RESEARCH USING HUMAN REPRODUCTIVE TISSUES.

2.(b) Is your research using human reproductive tissues conducted: (CHECK ALL THAT APPLY)

Directly by your company in Canada

Directly by your company or parent/affiliate outside of Canada Indirectly only (e.g., by purchasing research from or contracting with other organizations or individual researchers, or by grant funding) In collaboration with a partnership or consortium of Canadian companies

In collaboration with a partnership or consortium of companies in other countries

	participate financially or otherwise Other (PLEASE SPECIFY):	
Proje	rovide details of research projects, plect Form (last page of this quest cipate in directly or indirectly.	
	What is your company's approarch in which human reproductive ti	
	In Canada: \$ In ot	her countries: \$
devel	What is your company's approxima lopment in which human reproduct UDE AMOUNTS NOTED FOR QUES	tive tissue(s) is used? (DO NOT
	In Canada: \$ In or	ther countries: \$
your	Which human reproductive tissue company for any purpose during the T APPLY)	s have been acquired or used by the last 12 months? (CHECK ALL
Cana	ada Internationally	
		ova
		embryos
		ovarian tissue abortuses/fetal tissue
		placentas
		other (e.g., sperm) (PLEASE SPECIFY):
3. for h	Does your company have written parandling of human reproductive tissu	rocedures or protocols/guidelines ues?
	No	
	Yes> Please attach (including b	lank copies of any consent forms

or other protocols/guidelines for handling of human

reproductive tissues)

B. Sources of Human Reproductive Tissues

4. If your company, either in Canada or internationally, has received any human reproductive tissues, please indicate below the sources from which they were received, and the types of tissues received. (COMPLETE FOR EACH SPECIFIC SOURCE FROM WHICH HUMAN REPRODUCTIVE TISSUES WERE RECEIVED) (When identifying sources, please include all branches of your own organization.)

Name of contact person: _ City/province/country: _	FORMATION
Full name of organization: Name of contact person: City/province/country: Area code/telephone:	Name of area ova embryos ovarian tissue abortuses/fetal tissue placentas other (e.g., sperm) (SPECIFY):
Full name of organization: Name of contact person: City/province/country: Area code/telephone:	Name of area ova embryos ovarian tissue abortuses/fetal tissue placentas other (e.g., sperm) (SPECIFY):

Please photocopy this page if you need additional space to report on sources of human reproductive tissues, and attach.

5. Have you distributed or redistributed any human reproductive tissues to other organizations or researchers for any purpose in the past year, including disposal?

Yes
No ---> (ALL RESPONDENTS ANSWERING "NO" SHOULD GO TO SECTION D, QUESTION 7)

6. If you have distributed or redistributed any human reproductive tissues, please indicate below the recipients of these tissues, the types of tissues distributed and the use made by the recipient. (COMPLETE FOR EACH SPECIFIC RECIPIENT ORGANIZATION TO WHICH HUMAN REPRODUCTIVE TISSUES WERE DISTRIBUTED) Use the following codes for recipient use: "D" for disposal; "R" for research; "C" for commercial use; "0" for other; and "?" for unknown.

Types of tissues				
Distributed/redistribu		Recipient		
RECIPIENT IDENTIFICATIO	N INFORMAT		ch box	that
applies)		Use*		
Full name of organization: _		ova		
Name of Contact person: _		embryos		
City/province/country: _		ovarian tissues		
Area code/telephone: _		abortuses/fetal		
		tissues		
		Placentas		
		Other (e.g., sper		
		(specify):		
Full name of organization:		ova		
_		embryos		
and the contract of the contra		ovarian tissues		
Area code/telephone:		abortuses/fetal		
Area code, telephone.		tissues		
		Placentas		
		Other (e.g., sper	rm)	
		(specify):		

* If you indicated "other" for use of any of the above, please explain the details below:

Please photocopy the above chart if you need additional space to report on organizations to which you have distributed human reproductive tissues, and attach.

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- D. Policy, Ethical, and Commercial Issues Regarding Reproductive Technologies and Human Reproductive Tissues
- 7. What, in your assessment, is the market potential for new products which require research using human reproductive tissues and/or products manufactured using human reproductive tissues? (CIRCLE ONE)

Low 1 2 3 4 5 High

8. What is your estimate of the size of the market, in the next five years, for products developed through research using human reproductive tissues, and/or products manufactured using human reproductive tissues? (CHECK ONE BOX IN EACH COLUMN)

Canada

Internationally

minimal
millions of dollars
tens of millions of dollars
hundreds of millions of dollars
cannot estimate at all

9. What specific types of research involving human reproductive tissues are likely to be undertaken by your industry in the next five years?

10. What are the potential benefits of this research likely to be?

11. What are the potential risks or problems in conducting this type of research?

12. What obstacles exist for companies in Canada that wish to conduct research in these areas? (CHECK ALL THAT APPLY)

Federal government regulations (e.g., Health Protection Branch approvals)
Federal government policies
Provincial government policies
Canadian patent law
Other barriers (PLEASE SPECIFY):

- 13. In your view, what policy changes (if any) would be desirable to encourage research and development in these areas?
- 14. Is research and development in these areas expanding more rapidly in countries other than Canada (for example, where parent companies, affiliates, or competitors operate)?

No ---> (GO TO QUESTION 15) Yes

(If yes) Which countries, and why?

- 15. What moral/ethical issues does the industry have to contend with in dealing with research on human reproductive tissues?
- 16. Does your company have written procedures for ethical review of research involving human reproductive tissues?

Yes ---> Please attach No

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E.	C	Completion
н.	SHIVEV	Complehon

17.	If	you	have	any	comn	nents	on	the	que	estioni	naire	or	on	new
repro	duc	tive	techno	logies	that	you	woul	ld lil	ke t	o shai	e wit	th t	he	Royal
Comr	niss	sion.	please	provi	de the	m be	low.							

- 18. Please be sure to attach all protocols, related blank consent forms, and all project information, in your fax or in the return envelope provided. Finally, please provide us with your name, telephone number, and fax number for use in the event we need to re-contact you. Keeping a photocopy of the completed questionnaire for your files will be beneficial if any of your responses need clarification.

RESEARCH PROJECT FORM

Instructions:	Please co	mplete one	form for	each res	search project	(ple	ease
photocopy if				Indicate	"proprietary"	for	any
information y	ou are una	able to reve	eai.				

Brief description of research project: (attach summary if availa
Please indicate how the research project is conducted: (CHI
Directly by your company in Canada Directly by your company or parent/affiliate outside of Canada Indirectly only (e.g., by purchasing research from or contracting other organizations or individual researchers, or by grant fund In collaboration with a partnership or consortium of Canada companies
In collaboration with a partnership or consortium of companies other countries In collaboration with a university or foundation project in which participate financially or otherwise
Other (PLEASE SPECIFY):
Name(s) and Affiliation(s) of Principal Investigator(s):
Status of project: (CHECK AND COMPLETE ONLY ONE) Completed in the past 12 months
Now under way (Start date:; Projected finish date:
Planned for the next 12 months (Estimated start date:
Projected finish date:
What are/were the amounts of funding? (Include items such as
time and overheads.) (Attach additional list if necessary)

7. Types of tissues used for this research: (CHECK AS MANY AS APPLY)

Ova
Embryos
Ovarian tissue
Abortuses and/or fetal tissue
Placentas
Other (e.g., sperm) (SPECIFY):

This study benefited greatly from assistance provided by members, staff, and consultants of the Royal Commission on New Reproductive Technologies. SPR Associates would like to thank Ms Millie Bilsky and many others for their help. SPR would also like to thank Ms Margaret deGroh, who provided assistance in the refinement of the statistical presentations and related text.

The study could not have proceeded at all without the broader cooperation of the Pharmaceutical Manufacturers Association of Canada, particularly its President, the Hon. Judy Erola, who provided extensive background for the researchers on the pharmaceutical industry. SPR would also like to thank PMAC members and the biotechnology companies that completed the survey.

Their participation and support in no way indicates agreement with the analysis or conclusions, which is SPR Associates' alone.

Notes

- 1. M. Mullen, "The Use of Human Embryos and Fetal Tissues: A Research Architecture," in *Background and Current Practice of Fetal Tissue and Embryo Research in Canada*, vol. 15 of the research studies of the Royal Commission on New Reproductive Technologies (Ottawa: Minister of Supply and Services Canada, 1993).
- 2. The Emergency Drug Release program is intended to provide drugs that have not received a Notice of Compliance for Sale in Canada to medical practitioners for the emergency treatment of patients. Health and Welfare Canada may authorize the sale of a quantity of a new drug to a practitioner for use in the emergency treatment of a patient under the care of that practitioner. Because of the long delays in getting certain drugs approved in Canada, there is a fear among PMAC members that physicians may not use the EDR program appropriately.
- 3. For additional information see the Canadian Biotechnology Directory, 1990-91, Industrial Biotechnology Association of Canada.
- 4. One company told SPR that one indication of market potential for such products is the development of Ceredase, a drug used in the treatment of Gaucher's disease (a rare enzyme-deficiency condition, most common among but not exclusive to Jews of Eastern European descent). The drug, manufactured by Genzyme Biotherapeutics of Cambridge, Mass., is produced from a human placental derivative supplied by Institut Mérieux. Treatment is reported to cost between \$100 000 and \$400 000 per year, and Ceredase has been called "the most expensive drug in history." A spokesperson for Genzyme Biotherapeutics suggested to SPR that demand for this particular placental derivative is likely to outstrip the supply of placental tissue. Consequently, the firm planned to switch to a recombinant version of the extract in 1993.





Canada's School Systems: An Overview of Their Potential Role in Promoting Reproductive Health and Understanding of New Reproductive Technologies

Shannon and McCall Consulting Ltd.



Executive Summary

There is a need to change the knowledge and behaviour of young people with regard to their reproductive health; preventive measures taken now could reduce their potential need to rely on new reproductive technologies to bear children in the future. Schools should be one of many institutions to take on this challenge, primarily because it is when young people are at school that they are most likely to face pressure to become sexually active or to engage in unhealthy behaviour as a means to increase social acceptance. To be effective, however, school-based health promotion depends on cooperation among education, health, and social service systems at all levels. Most schools are already involved in teaching reproductive health to students, but existing programs are not doing enough. In particular, many programs do not make a distinction between informing youths and changing their behaviour, and many programs are offered in isolation from other elements, such as health services, that could increase their effectiveness. Schools also have the

This paper was completed for the Royal Commission on New Reproductive Technologies in September 1992.

opportunity to provide more information about genetics and reproductive technologies within human biology curricula, but teachers lack information and materials; as a consequence, these areas receive little or no coverage in science courses.

This paper examines the current and future potential role of schools in preventing infertility and increasing knowledge about reproduction and new reproductive technologies. It provides an overview of how Canada's provincial and territorial school systems function, and it introduces several key concepts and terms that must be understood and applied if schools are to play an effective role in promoting reproductive health. It also assesses current policies, programs, and services in the areas of sexuality education and science curricula and examines their effectiveness. Factors that increase the effectiveness of reproductive health instruction include: school board support and commitment through formal, written policies; effective, ongoing teacher training; social support systems reinforcing desired behaviour from both parents and student peers; reproductive health instruction integrated with health services; age-appropriate and relevant information delivered over a period of time rather than in one-shot events; and effective communication and decision-making skills as tools for changing behaviour.

Finally, the paper outlines how different participants in the schools system, from the federal government down to parents and community groups, can improve the effectiveness of sexuality education, and it provides a suggested framework for a school-based health promotion program.

Introduction

Purpose of the Paper

This paper is designed to accomplish two objectives. The first objective is to examine the current contribution of Canada's 12 school systems to promoting reproductive health in school-aged children and youth and to preparing them to face the social, ethical, and moral issues associated with reproductive technologies. The second objective is to examine how this role could be enhanced in the future.

Only publicly funded primary and secondary schools are discussed in this paper; students in post-secondary institutions (colleges and universities) and people who have left the school system are not included. As well, other informal and community-based ways to educate young people are not discussed in this paper.

Defining Public Expectations of School Systems

During public hearings and in consultations with key organizations, the Commission heard a wide range of groups and individuals call for the education system to play a greater role in promoting the reproductive health of youth. Equipping people with the appropriate knowledge, attitudes, and skills to protect their fertility, it was argued, would reduce the possibility that they would one day be faced with the physical, emotional, and economic costs associated with being infertile at the time when they want to bear children. It would also reduce their need to rely on new reproductive technologies in the future and generate substantial savings to the health care system. Further, schools can provide scientific knowledge and social development to help young people make responsible and ethical decisions about new reproductive technologies later in life.

Prevention of Sexually Transmitted Diseases

In particular, public health experts made an urgent appeal for schools to play a more active role in preventing sexually transmitted diseases (STDs) among youth, as these diseases pose risks to fertility. "It is much more cost-effective to provide free condoms to a teenager and support her in insisting on their use, than it is to try and help her conceive with *in vitro* fertilization when she is 30 and discovers that her tubes have been scarred by silent chlamydia."

While most schools have instituted some level of sexuality education (including acquired immunodeficiency syndrome [AIDS] prevention programs for specific grades), health promotion experts believe that in many schools not enough reproductive health education is provided. They argue that the increasing incidence of sexual activity among youth places them at risk for a number of unwanted consequences, including exposure to STDs.

The Canada Youth & AIDS Study showed that a significant proportion of adolescents are now engaging in sexual activity at an early age; approximately one-quarter of Grade 9 students and one-half of Grade 11 students have had sexual intercourse at least once. In fact, by Grade 11, a small minority — approximately 8 percent of males and 2 percent of females — have already had 10 or more partners (King et al. 1988). By the time youths reach university or college, three-quarters of them will have engaged in sexual intercourse.

While AIDS programs in schools and media coverage have increased adolescents' awareness of the risk of human immunodeficiency virus (HIV) infection and to some extent other STDs, this knowledge is not translating into safer sexual practices. Surveys show that about one-quarter of sexually active youths do not use any contraception (Canada, Health and Welfare Canada 1990, 7), and, among those who do, usage of barrier methods is low. The *Canada Youth & AIDS Study* indicated that only 25 percent of male college students with one partner used condoms consistently. For young women in relationships, an even smaller proportion — less than 20 percent of those with one partner and less than 10 percent of those with 10 or more partners — used condoms. The most sexually active women tend to rely exclusively on oral contraceptives, which do not provide protection against STDs (King et al. 1988).

These adolescent sexual practices can lead to a number of unwanted consequences, including pregnancy and resulting abortion or adolescent parenting and welfare dependence. As well, unsafe practices increase the risk of exposure to STDs, including AIDS, gonorrhoea, chlamydia, and herpes simplex.

A recent Statistics Canada study indicates that the rate of teenage pregnancies dropped by 17 percent between 1975 and 1989, from 53 to 44 pregnancies per 1 000 women aged 15 to 19 (Wadhera and Strachan 1991). While the reduced teen pregnancy rate in Canada is encouraging, it still translates to 39 000 teenage pregnancies each year - most of them unplanned. Health experts point out that this number of pregnancies is an indication of the number of sexually active teens who are not using any contraception and are therefore placing themselves at risk of exposure to a STD (Mitchell 1992). In fact, it underestimates, as those using hormonal birth control only are not protected.

There is a growing body of research data pointing to very high rates of STDs among young men and women. While gonorrhoea rates for all age groups have declined over the past decade, the rate among females aged 15 to 19 years (338 per 100 000) is higher than for any other age group for

either sex (Jessamine and McHale 1989).

Chlamydial infections are more prevalent than gonorrhoea among adolescents, as they also are for the general population. Rates ranging between 5 percent and 20 percent have been found in sexually active Canadian adolescents and young university women (Hanvey and Kinnon 1993). A study of 541 sexually active teenage girls attending a paediatric gynaecology clinic in an Ontario children's hospital over a one-year period found a chlamydia rate of 14.7 percent (ibid). In Alberta, chlamydial infection is notifiable, and 1989 rates for females aged 15 to 19 and 20 to 24 were very high — 2 529 and 2 143 per 100 000 population. respectively,² or about 2 percent of young women. These figures are generally considered to underestimate the real prevalence of STDs in youth. The numbers would be higher if adjusted for a denominator of sexually active individuals and if all cases were reported to health authorities.

While the precise contribution of STDs to infertility in Canada has not been established, it is estimated that up to 20 percent of infertility is linked to STDs (Hanvey and Kinnon 1993). Symptoms are often not apparent, particularly in women, and therefore may go unnoticed and untreated for a long time. In women, if gonorrhoea and chlamydia are not treated, the infections may spread to the uterus and fallopian tubes, causing pelvic inflammatory disease (PID). This disease causes scarring, increases the risk of ectopic pregnancy, and can ultimately lead to infertility. Gonorrhoea and chlamydia on very rare occasions may affect the fertility of males by causing scarring of the epididymitis, which can partially or completely block sperm transport (U.S. Congress, Office of Technology Assessment 1988, 61).

In their report "The Infertility Dilemma," the Canadian Advisory Council on the Status of Women estimates that if current rates of STD infection in young women continue, 20 percent will acquire PID by the age of 20. If nearly one-quarter of these young women become infertile, the rate of female infertility could increase substantially (Bryant 1990, 20).

Prevention of Other Health Risks

The Commission heard that while STDs represent a serious threat to the reproductive health of youths, there is a range of other factors — including smoking, alcohol and substance abuse, environmental hazards, and poor nutrition — that must also be considered. These factors are relevant for two reasons. First, they may contribute to some aspects of infertility (Hyndman 1993). While infertility may be far beyond the immediate concerns of adolescents, the adoption of lifestyles that involve one or more of these high-risk behaviours may have consequences for their health and well-being in the short term and also in the longer term. Secondly, research has indicated that youths who engage in one type of high-risk behaviour, such as smoking or alcohol use, are more likely to engage in other high-risk behaviours, such as sexual activity with a large number of partners (King et al. 1988, 94). Health experts suggested that if schools can effectively encourage youths to adopt healthy behaviours in one area, there may be positive dividends in other areas as well.

Changes to Science, Home Economics, and Ethics/Religion Courses

In addition to calling on the education system to promote reproductive health among youth, the Commission heard some individuals call for schools to provide information about human genetics and reproductive technologies within human biology curricula to enable young people to understand the role genes play in health and diseases and to assist them in making informed decisions about their reproductive options in the future. It was also argued that science courses should help youth to better understand the roles of science, technology, and medical research in modern society. It was pointed out, as well, that home economics and ethics/religion courses offer opportunities for the study of infertility and new reproductive technologies.

Big Challenge, Little Time

A review of the expectations that have been voiced for school systems reveals that they are being given a big challenge. Most of those who appeared during public hearings were not educators themselves, although many of them were involved in education-related activities in the course of their duties as public health officers or members of associations involved in public health issues. These informed outsiders think that school

systems, in partnership with other agencies and their communities, should be doing a lot more than they are already doing with respect to reproductive health education: "We see on a daily basis the results of ineffective or nonexistent educational programs in our schools, sexually transmitted diseases, unplanned pregnancies, HIV, the list goes on ... Improved education and prevention programs in our schools, in all of our schools, could have a significant impact on STD-related infertility, we believe."

But we have to set realistic goals for school-based reproductive health programs. This paper will show that it is realistic to expect schools to offer about 5 to 10 hours per year of sexuality education within a comprehensive health curriculum of about 50 hours' duration. This limited time will compete with the 5 000 hours students spend each year watching television, being with friends and family, playing sports, and attending other classes. Shamai and Coambs (1992) have pointed out the folly of expecting schools to change health or social behaviours unless there is a concerted effort from other agencies, parents, governments, and the community. Schools cannot do it alone, nor should they be expected to.

Thus, changes are needed in more than simply the instruction offered in schools. Health units can and should be expected to offer accessible sexuality clinics near or in schools. The media need to regulate advertising and programming. Schools and community organizations should mount programs to help parents talk openly with their children about sex. Provincial and territorial governments should provide adequate funding for coordinated programs. Universities need to change their curricula. The federal government needs to coordinate its many agencies, departments, and funding programs to promote reproductive health in a more coherent manner. In other words, we need a comprehensive approach using schools as a key setting within the community.

This paper will examine the role schools are currently playing in promoting reproductive health among school-aged children and youth, as well as relevant aspects of reproductive technologies in science and other curricula. It will also assess what role schools can realistically be expected to assume in an environment that is already pressing for schools to increase students' knowledge and living skills in a range of other areas.

Schools acting alone will not be able to change health-related behaviours. They need the support and involvement of parents, other professionals, health and social service agencies, community groups, media, and governments; therefore, the relevant role of these agencies is also discussed in this paper.

Research and practice have demonstrated that by linking school-based instruction with available and accessible health services, with social support from parents, peers, and the community, and with a healthy physical environment within the school, health-related behaviours, attitudes, and knowledge can be changed (Baldwin et al. 1990; Fisher 1989; Parcel et al. 1987). For this reason, a framework for school-based health promotion is explained and recommended as part of this paper (Canadian Association for School Health 1992a, 1992b).

Organization of the Paper

The body of this paper is divided into five sections. Section 1 describes how provincial and territorial school systems function, including their characteristics, financing, and the players and processes that influence what youths learn in schools. Some key concepts from education and health promotion are introduced here to facilitate discussion in later sections of the paper. Section 2 describes relevant subject areas and messages conveyed in schools that relate to reproductive health and new reproductive technologies. Section 3 identifies what is known about the effectiveness of programs designed to promote the reproductive health of youths. Section 4 identifies current trends in education that relate to reproductive health. Section 5 provides conclusions and suggests a number of recommendations the Commission may want to consider with regard to the role schools might play in promoting the reproductive health of youths and increasing their knowledge about new reproductive technologies.

Section 1. How Canada's Provincial and Territorial School Systems Function

This section will briefly describe the characteristics, financing, and structure of Canada's 12 provincial and territorial school systems and the key players who influence what students learn in schools. We begin by introducing some key concepts and terms from education and health promotion that must be understood and applied if schools are to play an effective role in promoting reproductive health.

Key Concepts from Health Promotion

The World Health Organization (WHO) definition of health is relevant: "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity." Health promotion is the science and art of helping people change their lifestyles to move toward optimal health. This change can be caused by a combination of efforts to enhance awareness, change behaviour, and create environments that support good health practices. Of the three, supportive environments will probably have the greatest impact in producing lasting changes (O'Donnell 1989).

A Canadian application of health promotion theory to schools has just been used as the centrepiece of a WHO (1992) statement on comprehensive school health. It defines school-based health promotion as "a broad spectrum of programs, activities and services which take place in schools and their surrounding communities." These programs, services, and activities are the responsibility of young people, families, professionals, health and social service agencies, schools, community organizations, the media, and governments at all levels. School-based health promotion

combines instruction about health, support services, social support, and a healthy physical environment.

Table 1 provides a checklist of the elements recommended with a comprehensive, school-based reproductive health promotion framework. Proponents of school-based reproductive health programs may find this framework useful as an assessment and planning tool. Otherwise, school-based efforts may rely only on instruction. The efficacy of an instruction-only approach has had mixed results in empirical studies and evaluations of sexuality education.

Table 1. Checklist of Elements for School-Based Health Promotion Framework

Instruction	Social support	Support services	Physical environment
comprehensive health curriculum lifestyle-focussed physical education mandatory home economics course health integrated into other subjects effective teacher inservice training pre-service teacher training adequate teaching/learning materials appropriate instructional methods opportunities for informal learning with parents and peers	role models peer support adult mentoring positive school climate staff wellness effective schooling healthy public policy media cooperation family involvement community involvement	appraisals screening services early identification child protection services referral procedures health services guidance services social services for students and families special education/student services treatment services where appropriate support during rehabilitation pre-service and in- service training for school nurses, guidance counsellors, school social workers, and school psychologists	alcohol use hygiene, lighting, sanitation, and other environmenta health standards

Success Depends on Cooperation

Effective school-based reproductive health promotion depends on cooperation among education, health, and social service systems at all levels. The description in Table 2 applies to AIDS/HIV but could be easily adapted and applied to reproductive health. The necessary cooperation has been described at the national, provincial/territorial, community, and neighbourhood levels.

Table 2. Levels of Cooperation Among Education, Health, and Social Service Systems

Level/type of cooperation Potential objectives Federal level

• Interorganizational cooperation

national non-governmental organizations and various federal departments, such as health and welfare, secretary of state, and justice

joint position statements, ongoing coalitions, regular communications, joint conferences, shared newsletters, more activist role for AIDS clearinghouse, joint projects or activities, joint organizations of public awareness programs

• Interdepartmental cooperation

units within departments, primarily within Health and Welfare Canada (HWC)

designated funds within the Social Sciences and Humanities Research Council of Canada (SSHRC), multi-cultural adaptations of educational resources

• Intergovernmental cooperation

collaboration between HWC and provincial/ territorial departments of health and education as well as the Council of Ministers of Education, Canada (CMEC) and the Advisory Committee on Community Health (ACCH)

increased use of HWC-CMEC agreement, significant dissemination of HWC-CMEC AIDS project results, improved connection with ACCH

Table 2. (cont'd)

Level/type of cooperation

Potential objectives

Provincial/territorial level

Interministry cooperation

collaboration among departments of health, education, and social services continuation of interministry AIDS committees: refinement of interministry policies; interministry agreements on sexual health services: evolution of AIDS policies to cover STDs, higher-risk populations, needle-sharing programs, etc.

Interorganizational cooperation

collaboration among non-governmental organizations and government departments

joint position statements, ongoing coalition, regular communication, joint conferences, shared newsletters, joint projects or activities, joint organization of public awareness programs, ioint review and refinement of AIDS curriculum, continued use of advisory committee on AIDS education and prevention

Interdisciplinary cooperation

professional associations and unions representing physicians, nurses, teachers, public health workers, social workers, and others

joint statements, development of minimum standards for agencies/ professionals

Table 2. (cont'd)

Level/type of cooperation

Potential objectives

School district/community level

Interagency cooperation

school districts, health units, social service agencies, and other agencies mandated by government to provide programs and services to youth joint project funding, shared funding of programs, joint in-service programs, staff loans, shared offices or services, joint program planning, regular meetings of administrators, written protocols, regular information sharing, joint record keeping, joint community awareness activities

Interorganizational cooperation

This community-based cooperation among mandated and voluntary agencies would not imply a shift in power or decision making within the community. Such cooperation might be in the form of a coalition or an advisory committee created by an agency or the school district.

joint workshops, statements, projects, or activities; joint community needs assessments and program evaluations; creation of joint coalitions or advisory committees; organization of joint community awareness activities; joint review and refinement of school district AIDS program; joint review of implementation of AIDS program

Community development

This form of cooperation would imply a shift in the decision-making process in the community through the creation and support of advocacy and self-help organizations.

School/neighbourhood level

• Interdisciplinary cooperation

This cooperation is among individual health, education, and social service professionals.

School/family/community cooperation

endorsement; support for selfhelp and advocacy organizations; in-kind donations of services, offices, and resources

joint-use management, record keeping, regular meetings

Table 2. (cont'd)

Level/type of cooperation

This cooperation could be in the form of participation in decision making or in instructional activities as a volunteer or at home with the child.

Potential objectives

information meetings for parents, review of educational programs or materials, use of home-based instructional activities, use of physicians and persons living with AIDs in class presentations, cooperation with local churches and service groups, regular programs on local media, development of AIDS policies by local employers, cooperation with youth and family organizations

· Intraschool cooperation

This cooperation among the principal, teachers, health teachers, guidance counsellor, social worker, school nurse, and other staff can create the in-school social support necessary for effective prevention.

school goal setting about AIDS and student health and information meetings on AIDS

Theories and Models

The theoretical basis for school-based health promotion has been well developed in the research literature. Parcel's (1984) discussion of school health research provides an excellent overview of the learning and behavioural theories that underlie school-based health promotion.

The research on psychosocial influences has coincided with a number of theories about learning and behavioural change (Flay 1986; Varenhorst 1984). Rotter (1954) and Bandura (1977) have developed a social learning theory that views learning as a reciprocal interaction among the individual. environment, cognition, and behaviour. Jessor and Jessor (1977) have explained, through their problem behaviour theory, that risk taking is a normal behaviour on the road to adulthood. Fishbein and Ajzen's (1975) theory of reasoned action makes important distinctions among an individual's attitudes, beliefs, behavioural intentions, and behaviour. They suggest that normative beliefs about what others think we should do, when combined with motivation, cause us to change our behaviour.

The interaction between the individual and the environment has also been analyzed. Communication theories led to a social inoculation theory that suggests that a limited exposure to a health/sexual problem can produce resistance skills (McGuire 1964). The concept of self-control suggests that an individual must learn to self-regulate, particularly over a protracted period of time (Kanfer 1977). Roskies and Lazarus (1980) have developed a coping theory describing the transactions between cognitive appraisal and the process of coping. This theory views coping as a pattern of responses that is saved as a resource to be expended in stressful encounters. Similarly, social competence models see social skills as a resource (Wine 1981). They differ from traditional defect models that try to identify weaknesses in individuals. Parcel and Nader (1977) argue that competence should be the basic outcome of health education programs. Social support theories view social support from the family and friends as a buffer and as a facilitator of behavioural change (Becker and Green 1975).

Perry and Murray (1982) developed an approach that considered the interaction between environmental influences (networks, the social system, and community norms) and personal influences (individual skills, perceptions, and personality).

Several models of health education and health promotion have been developed on the basis of these theories.

The Health Belief Model

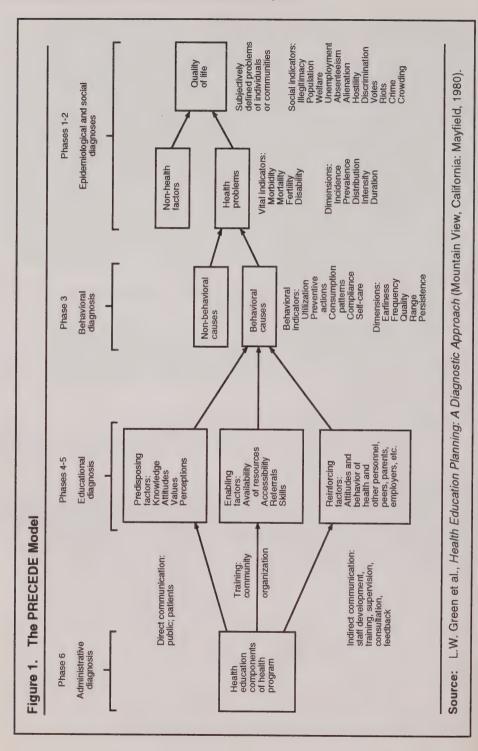
Janz and Becker (1984) suggest that an individual's perception of an ability to overcome barriers to his or her health is critical in adopting healthy behaviours. This model has more of a focus on health services than on health education.

The Risk Reduction Model

This adaptation of the Health Belief Model focusses on specific risks and on negating certain psychological, social, or economic factors that lead to risk (Catania et al. 1990).

The PRECEDE Model

The PRECEDE Model shifts attention away from the individual toward the environment. Predisposing, enabling, and reinforcing factors are taken into account in developing individual skills and behaviours (Green and Kreuter 1991).



Key Concepts from Education

Education Change, Reform, and Innovation

Education change is often poorly understood. Many people believe that schools have been changed when a new curriculum has been approved by the ministry of education. Later sections of this paper show how erroneous this perception can be. Education change is made up of three inseparable elements:

- materials (changes in curricula, programs, or organizational structures);
- practice (changes in the way agencies or professionals behave);
 and
- beliefs (changes in the organization's policies or culture or in individual attitudes, perceptions, or beliefs).

Fullan (1991) shows how these three elements must be integrated so that real changes in student learning can occur.

We should also consider the scope of education change. "Reform" and "innovation" are two terms used to show differences in the magnitude of education change (McCall 1982). Education reform implies major changes in budget and in the impact of school programs on student academic skills or their social development or in the structure and ideology of the schools. Educational innovations, on the other hand, do not affect the school's role in the socialization process, do not change the basic goals of schooling, and do not result in restructuring.

Introducing school programs on new reproductive technologies or to prevent infertility would be an educational innovation. However, such changes are linked to a larger trend — that is, reforming schools to play a greater role in preventing a significant number of health and social problems. A failure to incorporate education change theory into the planning and promotion of school-based reproductive health promotion will lead to frustration and inefficiency.

Curriculum, Instruction, Programs, and Teaching/Learning Materials

The terminology related to schooling is sometimes confusing. For the purposes of this paper, "curricula" are the documents approved by ministries of education stipulating what should be taught. "Teaching/learning materials" are the videos, textbooks, or computer software used in the classroom. "Instruction" is the methodology of teaching used. An instructional "program" is a combination of materials and instructional methods used to implement a curriculum.

Characteristics of School Systems

Each provincial school system is a multi-faceted entity with an extensive number of groups that are involved in some way in shaping what youths learn in school and at least 20 processes by which education

change can be implemented. The players range from those that have a formal role within the system, such as provincial ministries of education, school boards, teachers, and principals, to those that play an informal but often equally influential role from outside of the system, such as parents and communities.

The key characteristics of school systems can be captured in one sentence: they are open, loosely coupled bureaucracies (Konnert and Augenstein 1990). Each of these characteristics — openness, loose-coupledness, and bureaucracy — will have an impact on how reproductive health programs should be promoted, planned, and implemented.

Open

School systems are open to many external influences. Since schooling is a public service and since it deals with children, there are many safeguards built into the system that prevent any one interest group, point of view, or even government from exerting exclusive control over what children are taught. Because there are many players and processes involved, the education system can adjust to small changes but is slow to respond to significant change. Each innovation or reform must be negotiated and absorbed slowly into the system. This is not to say that significant change is not possible. It just takes a long time and a well-planned approach for that change to occur.

Social norms, public concerns, provincial/territorial politics, institutional cultures, community values, and professional norms and practices all influence the development of school programs. Inevitably, the points of view and self-interests are negotiated at every level of decision making. Rienzo (1989) points out that this process of negotiation is particularly true for sexuality education.

Loosely Coupled

Weick (1982) states that "schools are not like other organizations and they need to be managed differently." He describes school systems as being "loosely coupled."

Such systems are loosely coupled because the goals of education are indeterminate, the technology is not clear, ties among the people are loose, and individual schools must be responsive to a variety of sources, including the department of education, the school board, senior school district officials, local community values, and neighbourhood preferences.

Loosely coupled systems can adjust to small changes in their environments but are slow to respond to significant change. Such systems are more elusive, less definable, and harder to control. Administrative techniques rely on diffusion rather than direction, networks rather than hierarchies, and long-term change rather than specific projects. They require a focus on "professional socialization" rather than instruction. Broad goals, rather than managerial direction, are the glue that holds such systems together.

Bureaucratic

Another feature of school systems that is often ignored by reformers is that they are bureaucracies. Indeed, we need to be aware of the impact of four levels of bureaucracy in planning school-based reproductive health programs:

- the federal level, which pulls together the many departments, funding programs, and research agencies that deal with reproductive health;
- the provincial/territorial level, which coordinates the three ministries involved (education, health, social services) as well as the many different units within those ministries (e.g., curriculum, student services, finance, guidance, etc., within ministries of education);
- the community/regional level, which coordinates the policies, programs, and services of school boards, health units, and social service agencies; and
- the school/neighbourhood level, which coordinates the professionals within the school as well as in the neighbourhood.

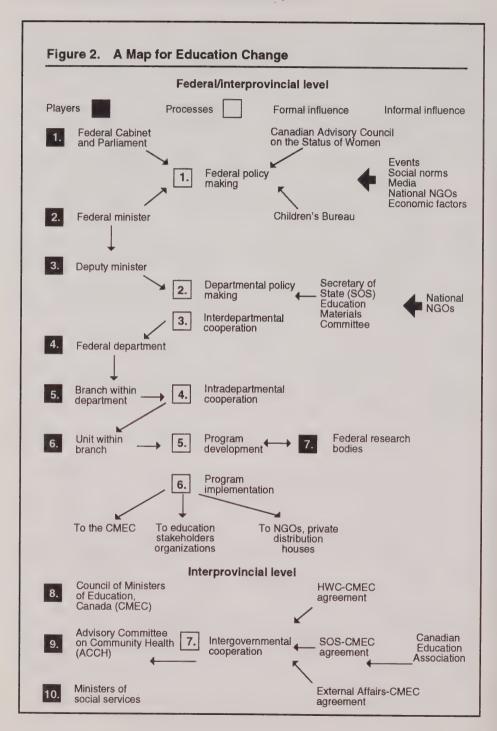
Initiating and Managing Change in School Systems

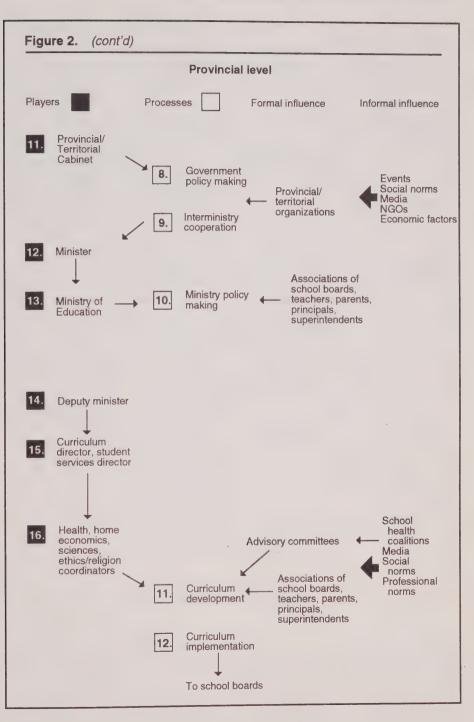
The characteristics of school systems require that any proposed innovation or reform be well planned, both strategically and operationally. Fullan (1991) and Maclure (1968) offer the following list of potential strategies:

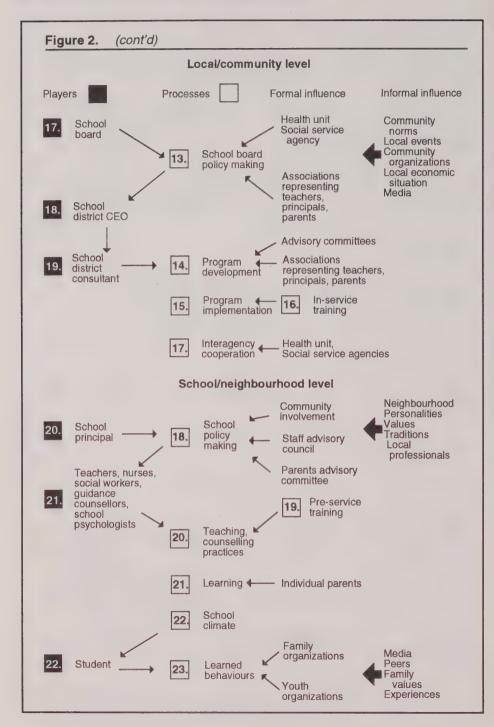
- creating a centralized planning group within a ministry or department;
- involving teachers as equals in the process from the outset;
- making extensive use of pilot projects;
- training a cadre of teachers and administrators;
- reorganizing administrative or organizational structures;
- encouraging school-community or school-university partnerships;
 and
- creating subsystems to promote change.

Indeed, Fullan recommends that reformers develop a "map" for their education change. Figure 2 presents such a "map" for promoting reproductive health programs in schools. The 22 different "players" and 23 different "processes" need to be considered carefully. As well, the numerous formal and informal influences on the decision making at various levels need to be assessed.

An understanding of this structure is essential to the success of promoting school-based reproductive health programs.







The Financing of Education in Canada

Canada has approximately 4.6 million children enrolled in its primary and secondary schools, and they are divided about equally between the two schooling levels. There are approximately 19 800 publicly funded schools in Canada.

There are about 900 school boards or districts in Canada. Many provinces have differentiated their school boards along religious or linguistic lines. Quebec and Newfoundland and Labrador use religion as the sole basis for school districts. Most provinces have a "public" system but also fund a "separate" Catholic system. Recently, New Brunswick and Ontario have funded school districts based on the English or French language. Quebec is considering a similar change. Some provinces also provide funding to independent or private schools, many of which are based on religion.

In 1989-1990, total expenditures on education in Canada, including colleges and universities, amounted to \$44.2 billion. Approximately 65 percent of this amount was spent on elementary and secondary schooling, representing an average per-student cost of \$5 790 per annum. Expenditure per student varies between provinces; the highest is in Ontario and Manitoba (approximately \$6 000), while the lowest is in the Atlantic provinces (\$4 660 and \$4 270 for Newfoundland and Prince Edward Island, respectively). However, the Atlantic provinces spend the largest proportion of their per capita gross domestic product (GDP) on education. This reflects the fact that GDP in these provinces is lower, so that even a relatively low expenditure per student translates to a greater financial burden for the Atlantic provinces than the same spending would represent for other provinces (Economic Council of Canada 1992).

In the current economic climate, it is not likely that new funding sources will be available to support better reproductive health programs; any resources allocated for improvements will therefore necessarily come

from within the current financial systems.

Fortunately, sexuality education is not more expensive than regular teaching. No expensive equipment or small class sizes are required — just good curricula, qualified and trained teachers, and relevant teaching/ learning materials.

The Structure of Canada's School Systems

Provincial Governments

Under Section 93 of the Constitution Act, 1867, Canada's provinces and territories have exclusive jurisdiction over primary, secondary, and post-secondary education. Educational policy is the responsibility of each provincial/territorial ministry of education, with certain responsibilities defined for local school boards. Despite this autonomy, the goals, educational trends, and problems of implementation in all provinces are similar in many respects.

Each ministry of education has a mission statement or statement of educational goals, which describes in broad terms the goals and objectives of education in that province or territory. The emphasis that is placed on promoting the health of students in these statements will reflect the degree to which health education and sexuality education programs can flourish within the system. In recent years, in response to new social and economic conditions, school systems across Canada have undergone a significant review of their basic goals. This subject is discussed in some depth in Section 4, which looks at trends within school systems.

In every province and territory, there is a set of educational policies in the form of regulations and directives, which school boards are mandated by law to interpret and implement at the local level. These regulations and directives dictate policies in a number of areas. Some school acts establish minimal service or funding levels and procedures for the provision of guidance, counselling, social services, and student services such as school psychologists and special education. Ministries of education also issue regulations or directives on the health and safety of their students. For example, directives or guidelines have been issued in all 12 jurisdictions on procedures to manage HIV-infected students or employees. Standards for physical environments in schools (health, lighting, air) may also be established in the school acts or in other legislation emanating from provincial health, environment, or municipal affairs ministries.

Occasionally, ministries of education sign agreements with other ministries about services to be provided to students. These services usually include psychological testing, health services, and social services. Generally, these interministry agreements cover one topic area at a time, such as child abuse. Most provinces and territories have developed interministry agreements on AIDS/HIV.

Each ministry of education has established a core curriculum that dictates what students must be taught (mandatory instruction) and ought to learn (optional instruction) in publicly funded schools. Program and curriculum policy comes in the form of curriculum documents. These documents tend to deal with knowledge-related requirements for student achievement. One of the primary difficulties for topics such as reproductive health, including STDs, is the need to focus on attitudes and behaviours in the teaching of these areas.

The curriculum development process in each province is very similar. There is a core curriculum, containing compulsory subjects such as English, math, health, physical education, and science. When an urgent public issue (e.g., AIDS) emerges, or when a review of existing core curricula is required, a committee is usually convened by the provincial ministry of education to recommend the goals, objectives, and program elements needed to address the issue or subject area. The committees or task forces are generally composed of teachers, administrators, university professors, and ministry personnel. Occasionally, school trustees and representatives from the community or business participate. There may

also be representation from other ministries, professions, or communities. These latter groups are usually represented when the health curricula are revised.

Curricula are reviewed every five to ten years. New units within the curricula are sometimes developed in response to crisis issues. AIDS and child abuse are two recent examples in health education. The AIDS issue. however, has forced a rethinking of many health education/sexuality education curricula.

There are provincial/territorial curriculum coordinators for health (sometimes combined with physical education), science, and sometimes home economics, who develop program units for their subject area. For example, health curriculum coordinators might develop smoking prevention programs tailored to each grade, including suggested lesson plans and teaching materials to be used. Each curriculum coordinator reports to a curriculum manager who oversees the entire curriculum.

Curricula vary by province in terms of their specificity and pedagogical approach. In Quebec, the provincial curricula (régimes pédagogiques) define learning objectives quite specifically by subject area. In theory, local school boards may vary program delivery, but they must adhere to the provincial objectives. In Ontario, there are no curricula, but rather guidelines that are very broad in nature. Local school boards are required to develop local curricula and programs that are appropriate for their communities.

British Columbia and Saskatchewan have based their curricula on a different pedagogy. Instead of traditional subjects and grades, their curricula are based on "integrated" or "common essential learnings" concepts. In British Columbia, for example, health is to be delivered in an integrated way with language arts.

It is important that reproductive health programs "fit" within the structures and pedagogical approaches of the 12 school systems in Canada.

Provincial/territorial ministries of education often assist school districts in program implementation. For example, most ministries provide support for health education by employing a health education curriculum coordinator and providing teacher in-service training, usually in the form of workshops lasting one or two days. Sometimes one contact person in each school district is trained. Ministries may also authorize, recommend, or fund educational material or resources, as they did quite extensively for AIDS education.

Other Ministries

More recently, provincial and territorial ministries of health and social services have begun to integrate their child- and family-related programs with their respective education ministries. Four jurisdictions are now using a health promotion framework (instruction, services, social support, and physical environment). Three jurisdictions are working on comprehensive interministry protocols to coordinate student-related health and social services.

Some ministries of health are upgrading their support for school-based health promotion. British Columbia, for example, has launched a Healthy Schools Program, which encourages staff and students to create and maintain healthier environments in the school. Often ministries of health or social services launch public awareness campaigns about health or social problems. Such campaigns are often not coordinated, in terms of timing, slogans, or content, with school curricula.

Provincial and territorial ministers of education belong to a group called the Council of Ministers of Education, Canada, or CMEC. Until recently, the CMEC had a low-profile role. Its decisions are normally made by consensus, and it is difficult to get 17 education and post-secondary education ministers to agree on priorities. However, there are recent indications that the CMEC will play a more active role at the national level. For example, its decision to develop a national mission statement for education might alter the dynamics in education at the national level. The CMEC's plan to develop the first national test of student skills in reading, writing, and mathematics is another example of this emerging role.

School Boards

The way in which curricula are taught, organized, and delivered is usually left to the discretion of local school boards or boards of private schools. The support of the school board is critical to the success of any educational innovation. The fact that the province or territory has decided on a policy or even mandated a curriculum does not necessarily mean that a school district program will be developed. On the other hand, when school boards are opposed to educational innovations, their opposition nearly always prevails.

School districts make important decisions about whether to adopt or oppose provincial goals and objectives and whether to add or reject optional units in the provincial curriculum. They may also decide to create new units that are missing from the provincial curriculum. They put together plans that define and address new knowledge needs, and they encourage the support of school principals for the change. They ensure that their schools have the necessary resources, including materials and in-service training, to implement the new or changed program, and they monitor implementation of the program.

Local school boards are governed by school trustees, who are elected by the public, usually for a two- or three-year term. The trustees oversee the school district's operation. School trustees influence curriculum development and delivery by bringing major issues to the board and to the school district administration in response to pressures exerted by parents and the community. They are frequently elected on platforms involving change to the education system. French immersion programs and parental involvement are two examples of issues that have been important in recent elections. School district administrators are thereby prodded to grapple with those issues. School trustees also play a formal role in curriculum

development in that they must approve all new or revised curricula that are developed by the school board administrators.

Every year most school board trustees participate in an annual retreat along with their senior administrators. These retreats usually produce formal statements on the priorities of the school district for that year. The administrative staff is accountable for ensuring these priorities are achieved. Many school boards establish comprehensive policy statements that describe expected results for programs and outline responsibilities and timelines for their implementation, as well as procedures for their evaluation. Often, however, this evaluation is poorly done because of the lack of priority that is given to it or mechanisms that ensure it takes place.

School boards usually leave some decisions about program content and methods to school principals and teachers. On sexuality education, the influence of principals and teachers, and that of parents, tends to be more significant. Committees usually must approve teaching/learning materials. A preliminary review of school board policies on sexuality education done for this paper found that most policies required that parental values were to be respected, parents were to be informed specifically about the program, and the provincial/territorial curriculum was to be followed.

Senior Administrators

Fullan (1991) states that the single most important factor in education change is how central office administrators support the process. Thus, support from school superintendents and health education consultants is critical to school-based reproductive health programs. (A dwindling number of school boards in Canada have health education consultants employed at the school district level to help classroom teachers.) This administrative support leads to an explicit, authorized implementation plan for education change, a vital part of the process.

Health Agency Programs

Health units and voluntary organizations in larger centres sometimes offer educational programs that involve schools. Calgary, for example, has a very effective sexuality program funded by the ministry of health. Ontario lists a number of health issues as priorities for prevention programs. In Quebec, the Centres locaux de services communautaires (CLSCs) play an active role in prevention. The degree to which there is coordination between school districts and local health units in delivering these programs was not determined by this project.

Availability of Health Services

The accessibility of sexual health services to adolescents is critical to the effectiveness of sexuality education. Such services are sometimes available in large urban centres but are non-existent in rural areas.

School Principals and Teachers

Although schools and teachers have a significant degree of latitude in deciding how they teach and what they emphasize, there are certain basic requirements they must satisfy in terms of course content. In sexuality education, there are usually formal requirements, which tend to be more explicit because of the sensitivity of the subject. As well, there is often a "hidden" and "evaded" curriculum, which reflects the local community's norms about sex as well as the degree of risk taking present within the school staff and administration.

The school principal is responsible for identifying and expressing a set of values and expectations that place a high priority on instruction in the total school program and ensuring that the subjects taught in classrooms meet the objectives established by provincial curricula and local board guidelines. Principals are also responsible for ensuring the overall quality of the teaching skills of teachers in their school and may provide guidance to teachers regarding how a specific subject or issue should be taught. For example, if the school board has mandated that elementary school teachers should teach reading based on a whole-language approach, then principals are expected to ensure that their teachers do in fact use this approach and to evaluate them based on this objective.

A national study of the actual behaviours of secondary school principals revealed that while most principals felt a strong need to provide instructional leadership, many lacked time or did not schedule time for that function (Thomson et al. 1990). A large percentage (at least half) operate mainly as administrators and as ad hoc crisis managers (Fullan 1982). The principal cannot be an expert in all subject areas for all grades. Teachers recognize the pressures and constraints placed on school principals and often prefer to seek the advice of their peers on instructional matters.

Teachers are a focus of educational change in that they can accept, reject, or modify the goals and philosophy of a program. Teachers can decide to use all or part of an optional new program. They can also decide whether to participate in recommended in-service training to improve their knowledge and skill in teaching a specific issue or subject. As well, teachers may play an important role as lobbyists, by advocating individually, or collectively through their associations, for new programs or for services, materials, social support, or school board policy to support the introduction or improvement of a program.

Parents and the Community

The local community — including parents, concerned citizens, "helping" professionals, and other groups and individuals — may also play a role in influencing what is taught in schools. In particular, parents are recognized as important participants in the educational process because they not only influence the scholastic success of their children, but may also lobby for the development of policies or programs. Parents exert influence either indirectly through their elected representatives at the

provincial or territorial level or directly on the school board. Parents may also serve on school advisory committees and school board committees; both may be involved in discussing changes to existing programs or the implementation of new programs. For example, in areas such as sexuality education, a community advisory committee is often used to recommend program goals, review teaching/learning materials, and provide feedback on the program.

Parents can also reinforce messages taught in schools and place them within a context that is consistent with their individual values and ethics. This aspect of parental involvement is discussed in Section 3 of this paper.

In the community, concerned citizens, including health professionals, can also play a role in determining what is taught in schools and what types of services are delivered. For example, the Ottawa-Carleton school boards decided to test the effectiveness of school health clinics after a community obstetrician/gynaecologist presented his concerns about local teen pregnancies to them. School health clinics have now been placed within key schools and are an expansion of the health education and birth control services provided by the region (see Section 3).

The Federal Government

Many federal departments and agencies develop programs and materials designed to address specific issues that are relevant to youths nation-wide, such as smoking, drug use, and AIDS. However, since provincial ministries of education have exclusive jurisdiction over education, the federal government does not have the legal power to mandate that provincial ministries of education adopt and implement these programs or materials. Often, however, federal officials may approach individual schools, usually by funding the production of teaching/learning materials by non-governmental organizations. This approach is problematic for several reasons. First, there is rarely an adequate understanding of the school systems and how they function. This often leads to a simplistic response, such as producing a video with no dissemination strategy, let alone having a process to promote educational change (see our earlier discussion of Fullan's work). Second, there is often an ad hoc nature to these activities, as departments fund several unconnected projects by non-governmental organizations that may or may not have adequate connections to the school systems. Third, the effort is rarely sustained for more than a year or two. The short project life leads well-meaning individuals to concentrate on reaching individual schools so that they can show immediate results. Often, people feel successful if their video or booklet is being used (actually they may only know if it has been sent) by 200 schools across the country. Even if 200 schools can be persuaded to respond to the initiative through incentive funding or distribution of materials, the remaining 19 600 schools are usually unaffected. As long as the artificial stimulus of funding or materials is provided, temporary change may occur in a limited number of schools. However, if the change is not institutionalized by the provincial school systems, it will not last.

In addition to developing educational programs and materials, the federal government funds research on issues related to education. Two examples are the recent report, *A Lot to Learn*, by the Economic Council of Canada (1992), which examines the way in which the education system prepares young people for employment, and the *Canada Youth & AIDS Study*. The federal government also organizes workshops and conferences. It provides funds to clearinghouses, which provide information to schools as part of their mandate. For example, Planned Parenthood has received funding for a clearinghouse to distribute materials on sexuality-related issues. The SSHRC and the National Health Research and Development Program (NHRDP) fund specific research on health, social, and education issues.

The legal use of the federal spending power has led to many federal departments creating divisions responsible for public education and training. The Canadian Teachers' Federation estimates there are more than 50 federal agencies, departments, or departmental units that may deal directly with schools across Canada. Hodgson (1988) reports that the federal government spends over \$9 billion per annum on education.

Some of the federal departments involved in public education include HWC, Agriculture Canada, Employment and Immigration Canada, Fitness and Amateur Sport Canada, and Environment Canada. Within each department there may be several branches or units with activities that relate to education, and some of these have activities and programs intended to educate youths. Within HWC, for example, the Laboratory Centre for Disease Control (LCDC) is sponsoring the preparation of guidelines for sexuality education, while the Education and Training Unit is responsible for liaison with schools. There is an internal committee within HWC to coordinate school-related prevention activities, but this committee needs to be strengthened if it is to be an effective vehicle for coordinating a reproductive health initiative.

Within federal departments, there are divisions responsible for communicating with the public. There is often a service function assigned to the departmental units responsible for education, which involves sending the content messages of other departments to the educational community.

Often, there is a miscommunication between those units responsible for education and those units responsible for the content of the issue, with both units trying to control the process to develop educational materials or programs. This may exacerbate the situation caused by attempts to bypass the provincial school systems to deal directly with the schools. The result is often a fragmented and ineffective delivery of educational messages to schools and school teachers.

Interdepartmental coordinating groups and agencies that may develop educational programs intended for youth include:

- Secretary of State (SOS) Educational Resources Committee. This
 committee meets to exchange materials and ideas for schoolbased programs.
- Minister of State for Youth. This office is supposed to have responsibility to oversee all matters affecting youth. In practice, the work of the office is dominated by the concerns of the senior ministry to which it is attached. Recently, this has been Employment and Immigration Canada.
- The Children's Bureau. This policy-focussed agency is devoted to welfare concerns of children and is interested primarily in the implementation of the recent UN Convention on the Rights of the Child.

Federally funded agencies include the National Institute of Nutrition, the Canadian Centre on Substance Abuse, the Canadian Council on Smoking and Health, the National Clearinghouse on Family Violence, the ACCH, and the CMEC.

One relevant example of an effective federal initiative in education is the AIDS Awareness Campaign. The AIDS program began with the creation of a separate administrative unit within HWC — the Federal Centre for AIDS. The separateness of the administrative unit led to many projects and activities being organized quickly. The Federal Centre for AIDS commissioned the Canadian Education Association, a group whose board of directors includes the deputy ministers of education (or their designates), to prepare a strategic plan to guide its work in supporting schools. Based on the needs identified by the Canadian Education Association, a range of educational materials was developed, including a school board policy guide for superintendents, an action kit for principals, a parent guide to discussing AIDS/sex with children, and several videos. An important aspect of the program was that effective partnerships were established with national associations representing school principals, superintendents, and parents to disseminate the materials. More recently, materials have been developed for specific target groups, including Aboriginal people, ethnocultural minorities, and post-secondary students.

As part of the AIDS Awareness Campaign, the Canadian Public Health Association (CPHA) was mandated and funded by the federal government to conduct a national education campaign. Unfortunately, the television advertising component of the public advertising campaign was never executed because the commercials met with resistance from broadcasters. However, the CPHA also conducted a series of national conferences and established a national AIDS clearinghouse, which now has an extensive collection of materials.

The AIDS issue provided the impetus for establishing a formal, ongoing liaison agreement between HWC and the CMEC. This working relationship enabled HWC to establish a significant research project concerning curriculum and teaching practice. Despite the very sensitive nature of the

issues it deals with and the traditional jurisdictional concerns, this HWC-CMEC AIDS/sexuality project will be able to evaluate the behavioural impact of a sample Grade 9 AIDS school program, as well as two different models of teacher in-service training. The preliminary results of this study will be available in December 1992.

Other National Players

There are a number of national organizations that may influence the educational programs and policies in schools. Some examples are provided in the following list:

- The Canadian Teachers' Federation adopts policy statements on issues. These statements are widely distributed and can have a significant impact on school systems. For example, a policy statement on AIDS was reproduced almost verbatim in many school board policies across the country. This organization is the best resource of the stakeholders in education.
- The Canadian Education Association, already discussed in the description of the AIDS initiative, is an excellent vehicle for developing consensus on national education goals without the formality of going through the CMEC. It is funded by ministries of education.
- The Canadian Association for School Health, a national organization representing 12 provincial and territorial coalitions, provides networks to reach provincial/territorial departments, professional associations, voluntary agencies, institutions, and community organizations. Groups such as Planned Parenthood are usually part of these networks and can use these coalitions to broaden interest in sexual health issues.
- The Canadian Association of School Administrators represents senior educational managers who act as gatekeepers to local school districts.
- Similarly, the Canadian Association of Principals represents school principals and can communicate directly with schools across Canada.
- The Canadian Home and School and Parent-Teacher Federation can reach parents across the country.

Section 2. Assessing Current Policies, Programs, and Services

This section describes the instruction and health-related services having relevance to reproductive health and new reproductive technologies that are being delivered in schools or in the communities near schools.

The information is drawn from several sources, including a review of existing literature, much of which was located in the library of the Sex Information and Education Council of Canada (SIECAN); an informal survey of curriculum coordinators in ministries of education; an assessment of current provincial/territorial curricula; and a preliminary search of the Canadian Education Association school board policy data base.

Aspects of reproductive health are generally taught within sexuality education programs, which may be called "family life" or "human growth and development" and are usually included in other courses rather than offered as separate courses. Sexuality education is usually offered as part of health education or (in the case of Ontario) physical and health education and may also be part of home economics courses. The biological aspects of human reproduction, which may include discussion of new reproductive technologies and/or genetics, are covered in science curricula. The moral issues associated with new reproductive technologies may be an area covered within family life, sexuality education, or religion/ethics courses. A discussion of each of these curriculum areas is included in this section.

An in-depth analysis of the adequacy and availability of sexual health services for adolescents was not possible in this project. A preliminary survey of ministry officials indicates that those services are not readily available. Yet research shows that when school-based instruction is combined with available and accessible sexual health services, adolescent behaviours change; when such services are not available, the impact of instruction alone has had mixed results. Similarly, it was not possible to assess whether all of the other elements of a comprehensive school-based reproductive health program are in place across Canada (see Table 1). However, we can sketch out a picture that is both heartening, because of recent progress caused by the AIDS issue, and frustrating, because of the immense challenges that still lie ahead.

Instruction

Across Canada, provinces and school boards have different names for sexuality education. For the purpose of this paper, reproductive health education is a major component within sexuality education. Existing curricula or courses tend to deal with reproductive health, sexuality, and personal development and relationships within an overall health curriculum.

Over the past decade, national surveys have shown an increase in the percentage of school districts with sexuality education programs, from 32 percent in 1975 to 57 percent in 1988 (Deiseach 1977; Ajzenstat and Gentles 1988, 7). This increase has been the function of a number of factors. The recognition of AIDS in 1981 provided a stimulus for curricula to be revised to deal with sexuality and STDs in a more frank and direct manner.

Groups such as Planned Parenthood and the Canadian Home and School and Parent-Teacher Federation have lobbied for the inclusion of sexuality education in school curricula. Gallup polls report consistently strong public support for school-based sexuality education; in 1984, 83 percent of the population favoured some form of sexuality education in schools.

Provincial/Territorial Curricula

Sexuality education is now mandatory across all provinces and territories from kindergarten to Grade 9 or 10, and most jurisdictions have recommended or implemented optional programs for Grades 10 to 12. An AIDS education unit, which usually includes some discussion of other STDs, is mandated (usually in the form of a specific unit) in all jurisdictions for Grades 7 to 12.

Despite public support for sexuality education and mandatory curriculum requirements across all provinces, commitment by individual school boards and schools to sexuality education remains uneven across the country. In most provinces, ministries of education have developed broad guidelines for sexuality education. However, local school boards are allowed to develop their own programs, with the result that there is a wide variation in course content and philosophical approach. School boards may develop guidelines on their own or may select and modify portions of existing guidelines and programs from other school boards in their province. They may even incorporate guidelines or purchase materials from other districts across Canada and the United States.

School Board Programs

A 1988 survey of school boards in British Columbia, Saskatchewan, Ontario, and Nova Scotia showed that 43 percent of them had not developed guidelines for sexuality education/family life programs (Ajzenstat and Gentles 1988, 7). However, in these districts, individual schools may take the initiative and develop their own programs.

Individual teachers and administrators are still forced to deal with controversial issues and community pressure without support or guidance from clear policy or procedures. In an informal survey, only half of school boards said they had written policy statements on sexuality education (see Appendix 2). Although the AIDS issue has prompted the development of new policies, most do not cover other STDs, reproductive health issues, or sexuality in a comprehensive way.

Politics continues to play a major role in determining which topics will receive coverage in school programs. Parental involvement and the active support of a community network largely predict whether there is adequate coverage of sexuality-related topics (Rienzo 1989).

Currently there is a lack of information about the status and quality of sexuality education in Canada, including the proportion of schools that offer it and the program content. The most recent research was conducted in 1988 and examined policies and programs in only four provinces

(Ajzenstat and Gentles 1988). The following overview of topics taught in sexuality education is based on that research, as well as an informal survey of ministry of education officials (see Appendix 2 for detailed results).

At the lower grade levels (5 to 8), topics taught most often include human reproduction and conception, interpersonal communications, family relationships, dating, and personal safety, including the prevention of sexual assault. (Family relationships and personal safety are also covered in early grades, starting in kindergarten.) Coverage of topics becomes more detailed and extensive in the older grades. About half of provinces mandate that contraception and STDs be covered in Grades 7 and 8.

Topics such as dating, teen pregnancy, contraception, AIDS, and STDs are usually covered in Grade 9. Nine of 12 provinces/territories provide extensive coverage of STDs within their mandatory programs at this level. Infertility, either as a consequence of STDs or in the context of human reproduction, and new reproductive technologies are rarely covered.

Most school sexuality education programs are founded on basic values, which include caring about oneself and others and becoming sexually intimate with another person in the context of a close, loving relationship, after understanding the responsibilities and possible consequences. Catholic schools are most likely to ground their teaching about human sexuality on Christian beliefs and values.

Sexuality or family life programs are usually designed to impart factual information within a broader context that emphasizes the importance of communication skills, encourages responsible decision making, and promotes the development of healthy attitudes toward sexuality. This pattern recognizes that providing youths with the facts without teaching them the necessary skills is unlikely to change their behaviour. This subject is discussed in greater detail in the next section.

An analysis of provincial/territorial programs/units specifically in relation to AIDS shows fairly consistent coverage of causes and transmission of AIDS, mutual monogamy, condom use, limiting partners, drug use, and support for persons living with AIDS. As well, programs focus on decision making, communication, self-management, and cognitive skills (King et al. 1988).

Teacher Training and Qualifications

The qualifications or training required for sexuality education teachers varies between provinces but in general tends to be minimal. A 1988 survey of school district requirements indicated that slightly more than half (56 percent) of the school boards in British Columbia, Saskatchewan, Ontario, and Nova Scotia that responded to the survey required in-service training for teachers. Only 5 of 115 school districts required specific university or teachers' college courses (Ajzenstat and Gentles 1988, 23).

There are 50 faculties of education in Canada that prepare teachers. Most of these education facilities require coverage of sexuality education for secondary school teachers who plan to specialize in health, home

economics, or physical education programs, but not for the generalist secondary school or elementary school teacher. Interestingly, home economics graduates are the most likely teachers to receive training in sexuality education that covers new reproductive technologies and STDs (Shannon and McCall Consulting 1990).

There was no attempt made in this project to assess the other aspects of effective instruction about reproductive health. Based on the author's

personal experience with AIDS education, it is likely that

• teaching/learning materials are not readily available on topics such as negotiating sex with partners, how gender inequities interfere with male-female communication about sexual issues, homosexuality, and STDs other than AIDS;

- parental involvement in instruction (via home-based activities and materials) is not widespread; and
- teacher in-service training to improve teaching methods relevant to sexuality education (active learning, "comfort levels" in dealing with sensitive issues, etc.) is not readily available the focus is usually on information.

Support Services

An informal survey of education ministry officials indicates that health services related to adolescents and reproductive health are not usually accessible to students. Only half of the respondents said that teachers were authorized to refer students to health clinics for counselling or information. Although those clinics were authorized to provide such information in three-quarters of the provinces/territories, many jurisdictions reported that services are not readily available outside the large urban areas. A national report on adolescent reproductive health concludes that such services are neither consistent nor universal (Canada, Health and Welfare Canada 1990). There is an interesting model in Ottawa-Carleton, where school-based health clinics are proving to be effective, but this model can only be dreamed of by most school boards.

Again, it was beyond the scope of this paper to assess the nature of health services. However, based on discussions with professionals in many provinces/territories, it is likely that

- adolescents who are sexually active are not systematically screened for STDs;
- coordination of referral procedures is done on an ad hoc basis and not by agreements between the local health unit and school board;
- the role of the school guidance counsellor in promoting sexual health is vaguely defined in policy or procedures; and

 school nurses, social workers, and guidance counsellors do not often participate in joint in-service programs.

Social Support

Public Policy

Information available to this author through an AIDS project and a newly started data base indicates that school board policies on reproductive health and sexuality are likely to be narrow in scope. The policies of health units and social service agencies were not assessed in this paper, but it is likely the situation is not much different from that of school boards.

Other Forms of Social Support

This project did not assess the degree to which schools and their communities provide other types of social support to adolescents with respect to reproductive health. Relevant questions would include the following:

- Have peer helper programs been widely used to prevent STDs and promote reproductive health?
- Do schools attempt to create a psychosocial climate that promotes health sexuality (e.g., discouraging verbal harassment of females about sex)?
- Do staff wellness programs address sexual health issues?
- Do local merchants cooperate with schools and public health officials in making it easy for adolescents to purchase condoms?
- Do local newspapers, community television, and radio stations support school-based reproductive health programs? Do they refuse advertising based on inappropriate sexual innuendos?

Physical Environment

The informal survey of education ministry officials indicates that very few schools in Canada have promoted reproductive health by installing condom dispensers within secondary schools. This simple change in the physical environment of the school can help to increase the likelihood of condom use by those who are sexually active.

Science Education

The Current Situation in Canadian Schools

A review of documents describing science education shows that curriculum designers are now seeking to connect the technical skills of science with societal values and concerns (Orpwood and Souque 1984; Science Council of Canada 1980). As a result, curricula and textbooks are moving toward a greater emphasis on "science and society" themes. This

new approach requires a less didactic, more open-ended approach to teaching, which many science teachers have not been trained to use. A study conducted for the Science Council of Canada (1991, 83) described an over-reliance on covering the material and finding the "right" answer. Some additional training of science teachers is required to encourage them to incorporate more open-ended discussions of the implications of areas such as genetics and new reproductive technologies in their science classes.

What Is Being Taught in Science Education

Human Reproduction and New Reproductive Technologies

An informal survey of ministry of education officials conducted for this paper indicates that human reproduction is covered in general science courses in junior grades (9 to 10) as well as in optional senior biology courses. Areas such as biotechnology and new reproductive technologies are not covered at the junior level, but senior biology courses in many cases have extensive coverage of these topics, as well as more in-depth coverage of human reproduction.

Genetics

The Science Council of Canada examined coverage of human genetics in health and science curricula in their report *Genetics in Canadian Health Care.* They noted that "all Canadians should leave the public school system with a basic understanding of the important human biology (including genetic), environmental, lifestyle, and health care factors that affect health. This knowledge would serve as a framework to help individuals maintain their own health, and to understand the changes in health sciences and technologies that will occur during their lives. At present most Canadians do not leave the school system with this knowledge" (Science Council of Canada 1991, 83).

The majority of high school students receive little or no instruction on the role genes play in health and disease, because current health and science curricula up to Grade 9 provide little coverage of this topic. While revised biology curricula for senior grades are starting to reflect advances in genetic science, many students drop science or drop out of school in later grades, and less than a quarter of students aged 15 to 19 years opt to take biology courses (Science Council of Canada 1991, 84). While studies have shown that adolescent girls are less likely than boys to take physics and chemistry courses, female participation in biology courses at senior levels is actually higher than male participation (Ferguson 1982, 26).

There have been many recent developments in genetic knowledge and related health care issues that are not reflected in provincial curriculum objectives or school board programs. While in theory curriculum reviews are to be conducted every five to eight years, in practice longer intervals are common. For example, the biology curriculum in Saskatchewan was developed in 1971 and is only now being revised (Science Council of Canada 1991, 84).

Even when genetics and health-related issues are included in provincial curricula, teachers often lack the information and resources to teach the topic. Textbooks tend to be outdated, reflecting both the small market for Canadian textbooks and the pace at which our knowledge of genetics is increasing. The fact that genetic knowledge and issues are so new means that teachers themselves often lack information and training to deal with the areas. The Science Council report (1991) notes, however, that both teachers and students are interested in the health and social issues associated with human genetics, and excellent courses have been developed when local medical genetics centres have provided resource materials and professional development for teachers.

Home Economics Education

As societies redefine themselves, schools often respond to the resulting changes in family structures with increased attention to home economics or family sciences education; they search for new definitions of "family." This situation appears to be occurring in Canada in the 1990s — for example, in 1990, a review of prime-time television listings revealed 27 different "family" shows, from *The Cosby Show* to *Roseanne*.

Many provinces now require home economics instruction for all students (male and female) at the junior high school level. An informal survey of ministry of education officials indicates that infertility, STDs, and new reproductive technologies are not covered in mandatory programs, although optional units may provide some instruction. In the senior grades, optional courses offer extensive coverage of infertility, adoption, STDs and their prevention, and new reproductive technologies. For example, New Brunswick's Family Living course outline has learning objectives that cover artificial insemination, surrogate motherhood, and *in vitro* fertilization. Manitoba's Family Studies Program has similar objectives. However, the majority of students do not opt for home economics courses in senior grades.

Ethics/Religious Education

The only information regarding ethics and religious education comes from the informal survey of ministry of education officials conducted for this paper. It reveals that some ethics or values courses in public schools cover new reproductive technologies and are likely to examine the ethical and moral issues related to them. In public schools, religion courses are optional or non-existent.

Section 3. The Effectiveness of School-Based Reproductive Health Programs

This section provides an overview of what is known about the effectiveness of school programs that are designed to promote the

reproductive health of youths, either directly or as part of broader health education initiatives.

The Impact of Sexuality Education on Adolescent Knowledge and Behaviour

Research suggests that a well-executed reproductive health program, when combined with other elements such as accessible health services and parental support, is capable of increasing adolescents' knowledge and awareness of reproductive health issues and positively influencing their sexual behaviour so that pregnancy or STDs are less likely to occur. However, there does not appear to be empirical research that conclusively proves that such programs result in reduced rates of sexual intercourse among teens or a lower incidence of STDs.

There are many reasons for this. For example, school boards and schools typically evaluate their sexuality education programs by gathering feedback on the program from teachers, students, and parents. A few school boards claim to study pregnancy rates in their area (Ajzenstat and Gentles 1988, 30). However, it is difficult to draw reliable conclusions about the effectiveness of a school's program based on these rates, as there are environmental factors outside school programs that contribute to the knowledge and behaviour of adolescents. Rigorous studies that compare a test group to a control group are therefore difficult to conduct.

The Canada Youth & AIDS Study found that in provinces where AIDS and STDs are mandatory elements of the curricula, knowledge scores among students were higher (King et al. 1988, 43), but across all provinces there is substantial room for improvement. Despite the existence of AIDS and sexuality education in many schools, the study indicated that most adolescents are still not well informed about STDs. Canadian youth know that HIV can be transmitted from one person to another through sharing drug injection needles and through sexual intercourse. However, a significant proportion (approximately 40 percent) of them do not know that using condoms and spermicides can protect them and their partners against HIV infection, and they know even less about how to protect themselves from other STDs.

Most youths believe that the chances of contracting a STDs are low. The report notes that "this explains in part their willingness to engage in unprotected sexual intercourse. Because most do not believe their own sexual behaviours could put them at risk of contracting a STD, they do not seriously contemplate either abstinence from sexual intercourse or protecting themselves or their partners, even most of the time, when having sexual intercourse" (King et al. 1988, 133).

One of the challenges facing educators who are involved in teaching reproductive health to youths is to ensure that awareness and knowledge of sexuality-related issues translate to safe behaviour. Specifically, educators need to make a distinction between creating awareness or

informing youths and actually changing their behaviour. Many health education programs aimed at simply providing information to students have failed to change adolescent behaviour because they are not based on this distinction. Kegeles et al. (1988) studied changes in the perceptions and in condom use of sexually active adolescents aged 14 to 19 years after they were exposed to intensive education in a large American city, where media and school coverage of the AIDS epidemic was high. Awareness of the effectiveness of condoms to prevent HIV transmission was high, but no increase in the actual use or intention to use condoms occurred.

Programs designed to promote adolescent reproductive health must recognize the barriers to changing behaviour. For example, factors associated with not using a condom include embarrassment about the purchase of condoms, difficulty discussing condom use with a partner, insufficient knowledge of STDs, and the belief that condoms interfere with pleasure. It has also been suggested that "young people in many instances take unwarranted risks because they are convinced that the consequences 'can't happen to me.' Thus, even sexually active young men and women who acknowledge their behavior may not take adequate precautions to prevent HIV transmission ... Young people tend to take their health and future for granted and believe that the absence of any symptoms today signifies a permanently healthy tomorrow, without any hints of mortality" (Keeling 1987)

Factors That Contribute to the Effectiveness of Reproductive Health Programs

This section elaborates on some of the elements of a comprehensive approach to school-based reproductive health promotion.

A review of the existing research on reproductive health education and consultations with those involved in adolescent health promotion suggest that the following factors increase the effectiveness of reproductive health instruction:

- developing formal, written policies on sexuality and family life programs by school boards to ensure that teachers understand the objectives and content of such programs;
- promoting effective, ongoing in-service teacher training to ensure that teachers are knowledgeable about subjects and are provided with suggested approaches to dealing with difficult, and often controversial, subjects;
- strengthening social support systems to reinforce the desired behaviour (from both parents and student peers);
- combining reproductive health instruction with health services;
- delivering age-appropriate and relevant information over a period of time, rather than offering it in one-shot events; and

• emphasizing communication and decision-making skills as means of changing behaviour.

School Board Policies and Resources

A Planned Parenthood report on sexuality education in Canada noted the importance of obtaining school board support and commitment for family life programs to ensure their implementation. The family life program coordinators who participated in that study indicated that "all efforts seemed to have failed until it became Board policy — which pushed reluctant administrators and principals to really act" and that "having a policy allows teachers to get on with the job of teaching — knowing that they have the support of the Board and resources necessary to do a good job" (Nolté 1984, 14)

An informal survey of ministry of education officials in all provinces and territories indicated that about half of school boards have written policy statements on sexuality education. Many used an advisory committee consisting of teachers, parents, school board representatives, and health professionals to develop these policies. Involving different groups from within the school system and community helps to ensure the broadest support for the program.

In-Service Teacher Training

The Planned Parenthood survey also indicated that many teachers felt the need for more effective in-service training to keep them up-to-date on relevant issues and available resources. Teachers who lacked formal training in this area felt that in-service workshops would make them more comfortable dealing with the subject matter.

At this time, in-service training of teachers in sexuality/AIDS/STD education is minimal and is not based on current theory. One-shot workshops are typical and are largely ineffective, as they usually fail to address individual needs and concerns. The majority of programs involve teachers from many different schools, but there is little recognition of the different environmental factors that exist in their own communities. Researchers have found that pre-service teacher education programs lack overall coherence, and the purposes of many courses are complex and unclear (Fullan 1991, 108).

A literature review indicates that effective in-service programs for AIDS and sexuality education in general include the following characteristics:

- Initial training should be provided to convey technical information, address gaps in teacher knowledge, and teach communication skills ("AIDS Education" 1989).
- Skills in working with professionals and agencies such as health clinics should be developed, as should skills in evaluating education material (Kerr 1989).

- The benefits and barriers perceived by teachers in teaching AIDS/sexuality education should be addressed, including their perceptions of the adequacies of their preparation, their expectations of student responses and social supports, and their willingness to teach the course (Levenson-Gingiss and Hamilton 1989).
- Classroom management techniques for dealing with sensitive issues should be taught, including how to answer personal or controversial questions (Rowling 1987; Wagman and Cooper 1981) and techniques for involving role playing in the learning process (Lawrance et al. 1990).

Parental Involvement

Parental involvement in both the development and implementation of reproductive health programs is crucial in several ways.

First, parents can play an important role by expressing support for sexuality education and engaging in a dialogue with schools about the types of messages to be conveyed and the context in which they should be expressed. Those involved in school reproductive health programs point out that it is essential that schools consult with their communities and provide information about the program or health service they would like to implement, so that the affected community has sufficient factual information upon which to make an informed decision about whether the school should proceed with the program.

Secondly, parents can reinforce the messages at home and place them in the context of their own values and beliefs. Parents remain important sources of information to children: studies show that approximately half of adolescents seek information about sexuality-related issues from their parents, among other sources (Baskerville et al. 1991, ii). However, some parents may be less informed about the issues than their children. Materials that describe the messages to be taught in school programs can make parents feel more comfortable about their ability to deal with the issues and more knowledgeable about the subject areas.

Eight of 12 ministry of education officials across Canada claimed that the sexuality/family life programs in their province or territory included material or information for parents (see Appendix 2). This information was probably prepared by local school boards. Some schools offer information evenings or special interviews, and a few school boards even offer a sexuality education course for parents (Ajzenstat and Gentles 1988, 26).

There is concern, however, that traditional parental involvement programs are not reaching those families and children who are most at risk. Difficulties relating primarily to socioeconomic status may hinder schools from communicating effectively with some parents. For example, one study showed that in areas with higher concentrations of families with low socioeconomic status, few parents claimed to have received a newsletter

about the school's health education program that was sent home with their children, although the program coordinators were confident that the children had received them. Among the parents who did receive the newsletter, only 22 to 33 percent found the information useful and reported that it promoted family discussions about the topics. Among parents of higher socioeconomic status, 92 to 100 percent found that the information was useful and promoted family discussions (Cogdon and Belzer 1991, 9). These findings illustrate the need for special efforts to reach some groups of parents.

It should be noted that parents are not the only individuals who can provide important social support for school programs. Churches, business leaders, health care professionals, and other individuals and organizations in the community may also provide input in the development of school programs or reinforce messages taught to youths. Like parents, churches can play a significant role by imparting messages about sexual behaviour in a context that promotes positive values, such as care and respect for others.

Health Services

Research studies have shown that instruction in preventing health problems can be effective in transmitting knowledge. However, when instruction is linked to other means employed in a health promotion strategy (support services, social support, and healthy physical environment), the behavioural change is much more significant. Combining reproductive health instruction with easily accessible health services will have a significantly greater impact on adolescent sexual behaviour than reproductive health instruction alone (Zabin 1986).

One jurisdiction that has moved in this direction is Ottawa-Carleton, where the regional health department has established five school-based sexuality health centres in high schools as one component of their Healthy Sexuality Program. The program was set up because research studies indicated that an increasing number of adolescents in the region were becoming sexually active at an earlier age, and a substantial proportion were not using contraception. "The purpose of the program [was] to increase access to information, services, and resources that enable the development and maintenance of healthy sexual behaviours in young people" (Baskerville et al. 1991, 2).

The school-based sexuality health centres proved to be effective in improving students' knowledge of contraception and STD prevention and had a positive impact on student attitudes toward healthy decision making. As well, birth control use significantly improved. The overwhelming majority (97 percent) of students who were exposed to the sexuality health centres found that the service was helpful. It should be noted, however, that the majority (81 percent) of students who sought counselling at the sexuality health centres were already sexually active the first time they

visited the centre, indicating that health centres are unlikely to play a role in influencing students' decisions regarding whether or not to become sexually active (Baskerville et al. 1991, ii).

In Ontario, there is concern among those involved in promoting adolescent reproductive health about the impact of Bill 109, which is before the Ontario legislature, on providing accessible health services to youths. Individuals would have to be 16 years old to be eligible for medical treatment without parental consent. This bill, if approved, would represent an impediment to sexually active youths in gaining access to birth control counselling and STD treatment in Ontario.

Program Delivery

Delivering information that is meaningful and relevant and presenting it in a context that focusses on communication and decision-making skills can increase the likelihood that programs will change adolescent behaviours. Health promotion experts claim that too often the materials used in sexuality education programs are neither relevant nor compelling to youths. What Bill Bowie said at a recent conference is representative: "What is in a lot of the AIDS teaching material is a diagram of the HIV virus. What difference does that make in terms of how people behave? It is often incomprehensible, it is often scary, and the guilt and anxiety that it can produce can interfere with the ability to learn. But also if we tell people that having sex means that an absolutely dangerous, awful, horrible thing is going to happen, and they have sex and nothing nasty happens, we are reinforcing their scepticism of what we teach them."

One of the greatest challenges in teaching reproductive health to adolescents is how to translate knowledge into appropriate behaviours. Teaching youths to adopt behaviours that will reduce the chance they will be exposed to a risk that they cannot see and have no personal experience with is a hard sell.

Even if youths do acknowledge that STDs pose a potential threat to their health and well-being, social factors may make it difficult for them to engage in safe behaviours. In particular, young women may find themselves pressured by their partners to be sexually active or may experience resistance from them to using a condom. Young men feel pressures to become sexually active as a means of increasing their social acceptance with peers.

Effective school reproductive health programs incorporate components that take account of these barriers to behavioural change. The effective programs provide adolescents with important tools, such as decision-making and communication skills, to help them make responsible choices and stick by them. Youths can be encouraged to anticipate upcoming sexual intimacy with a partner and to make decisions about sexual limits and preventive measures before the situation arises. Teaching them sexual negotiating skills can better equip them to say "no" to a

partner or to insist that they use appropriate contraception. Studies have shown that school programs that teach communication skills are more likely to result in safer sexual behaviours.⁷ The use of role play and behavioural rehearsal to practise skills can help students develop a repertoire of preventive responses.

Not surprisingly, the extent of exposure youths have to sexuality education influences their knowledge level and behaviour. High-intensity programs that are repeated over a period of time are more effective than single, low-intensity sessions (Rotheram-Borus et al. 1991). This is true not just for sexuality education, but for health education in general. An American study revealed that students who were exposed to multiple health topics over a period of several years in school were less likely to engage in high-risk behaviours (e.g., smoking, alcohol use, drug use, riding with a driver who has been drinking) than those who received only one year of health education (Louis Harris and Associates 1988). The same study also found that there was only a small difference between the attitudes and behaviour of those who had one year of health education and the attitudes and behaviour of those who had none, further reinforcing the need for continuous education over a period of years.

Fifty hours of effective health instruction per year has been proven to be effective in changing health behaviours (Connell et al. 1985), and this would be an excellent standard for many schools in Canada for well-implemented health instruction. There has been considerable progress recently made in mandating such obligatory instruction in provincial/territorial curricula. Realistically, 20 hours of instruction in sexuality education per year would be a generous allocation of the scant health instruction time available in schools. It would probably be realistic to assume that 10 of those 20 hours could be devoted in some way to messages about reproductive health, including abstinence or safe sexual behaviours.

School-Based Health Promotion

At least four educational jurisdictions now have explicit policies that favour a comprehensive approach to school-based health promotion responding to health or social problems affecting children and youth (see Appendix 3). This trend to a multi-issue, integrated approach is very new and reflects the growing belief that education and health are inextricably linked. "Young people who smoke and drink often experiment with illegal drugs and early, unprotected sex as well. These same young people are also prone to school failure" (Carnegie Council on Adolescent Development 1989).

Professionals involved in health promotion believe that a comprehensive approach to school health is more effective than dealing with health-related problems in a single-dimensional way. They maintain that health instruction should be integrated with school services and the

students' environment and coordinated with community efforts. Implementation of programs is most effective when they are the joint responsibility of a coalition of school and community health educators and other interested individuals such as parents.

The Dartmouth Health Promotion Study is an example of how a comprehensive school health promotion program was implemented. The study identified two priorities — the need to "(i) reduce cardiovascular risk factors such as high consumption of sodium, fat and sugar, low levels of physical activity and smoking and (ii) promote mental health, with particular attention to enhancing self-esteem and coping with stress" (Cogdon and Belzer 1991, 7). These two objectives of the program were addressed with a variety of strategies such as replacing unhealthy snacks in the school cafeteria with "heart-healthy" cookies, teaching children about smoking and nutrition, providing parents with materials with which to reinforce lessons taught at school, and involving parents and community members in the delivery of stress management lessons to the children.

While quantitative research results are not yet available, parental response has been very positive. Many parents claimed to have noticed improvements in their children's eating habits, physical activity, and self-esteem.

Despite the evidence to support the effectiveness of a comprehensive school health approach, there are barriers to the implementation of such programs. One of these barriers is the tendency of some people to view health instruction as an add-on that detracts from a more proper emphasis on the three Rs. Health and reproductive health programs will have to compete with other public concerns such as literacy rates, school dropouts, scientific achievement, and global economic competition. The trends and competing issues within the school systems in Canada are discussed in the next section.

Section 4. Trends in Education

The Functions of Schooling

Schools perform five basic functions for society:

- 1. They provide basic literacy and numerary skills for all students as well as preparation for further academic study in post-secondary institutions for some students.
- 2. They prepare youth for the world of work.
- 3. They socialize young people in the dominant norms, ideologies, and cultures.
- 4. They maintain custody of children during the day.
- 5. They sort and select students for their future place in society.

These functions are always performed by schools for their respective societies. The nature of the society will determine the emphasis to be placed on each of the functions. Whenever a society transforms itself, as we are doing in Canada in response to the post-industrial age of the twenty-first century, these functions of schools are changed. The Russian launch of the Sputnik satellite in 1957 marked the point when the functions of schools in North America were called into question. The Hall-Dennis Report in Ontario, the Parent Commission in Quebec, and the Chant Commission in British Columbia all reflected that reform period in Canadian schooling.

We are once again at the point when the functions of schooling are being reviewed. Indeed, commissions of inquiry have recently been completed or have been under way in Quebec, Ontario, Newfoundland, New Brunswick, Saskatchewan, and British Columbia.

In order to understand some of the societal concerns with which reproductive health will have to compete to gain a greater place within the school system, let us review the new pressures on the five functions of schooling. This discussion will compare the schools of today with those of one generation earlier.

Literacy, Academic Achievement, and Lifelong Learning

Schools were expected to provide basic literacy and numerary skills to *some* students. The 50 percent of students who dropped out of school were expected to find unskilled jobs, which nevertheless usually provided adequate levels of income. Most students were English-speaking by birth, and fluency in one language was considered adequate.

Today, schools are expected to provide *all* students with basic literacy skills. Significant numbers of students do not have English or French as their first language, although many of them and many other students aspire to having fluency in both French and English when they graduate. Students today need to have learned computer skills before they can graduate. Students who left schools in previous generations are now expected to graduate (about 70 percent do). As well, there is a rapidly growing amount of knowledge to be transmitted. Traditional academic disciplines are crumbling under the weight of information overload. Curricula are being "integrated" in an attempt to teach several things at once. Whereas students could once expect to end their formal education at one point, now schools must instil lifelong learning skills. The three Rs are no longer sufficient.

Vocational Preparation

Global economic competition is placing pressure on schools to increase their academic standards so that the capable students achieve more while also ensuring that students experiencing difficulty achieve basic levels of competence. The job market is unpredictable, so schools must teach

higher-order skills such as critical thinking, decision making, and interpersonal communication. The Economic Council of Canada (1987) has called for changes to schools, and various international comparisons are used to urge other changes that are being promoted by Canada's business community.

Socialization

At the same time, schools are being asked to assume more of the role of parent and pastor, as adults fail to transmit what one author has called "social capital" to the young. Single parents and dual working parents have less time to socialize their children. The influence of religion and churches has declined. The social consensus of homogeneous communities has been replaced by diversity and discordance. Schools are now seen as one of the few places left for society to transmit its common values. Public concern about health and social issues such as AIDS, family values, drugs, and suicide has skyrocketed. Politicians respond with new, mandatory programs. Reproductive health is one of those concerns that are transforming schools into what Cleary and Gobble (1990) have called a "social agency." Ministers of education are responding with expanded and improved health curricula. The public's concern about the environment is just beginning to be expressed in school systems. An international comparison shows Canadian children are least likely among 11 industrialized nations to experience good communications with parents and friends (King and Coles 1992). Other studies show young women experience daily frustration and conflicting expectations because of their gender (Robertson 1990).

Custody

The impact of raising the age for compulsory school attendance to 16 has already been felt in this generation. Pressure is now on to provide schooling to younger children in the form of daycare. Disabled students, previously excluded from regular schools, are now expected to be taught in regular classes.

Selection

The selection function of schooling is rarely discussed openly. Yet all societies, whether capitalist or communist, use schooling to help young people find their place in society by awarding various credentials. Students arrive in schools with unequal life chances based primarily on socioeconomic status. Our ideology of providing equal educational opportunity is being questioned in a society where the differences between rich and poor are widening. Schools are now being asked by many groups to provide equal results — something that is clearly impossible.

Reproductive health programs will have to compete with all of these new pressures on schools.

Political Change

The role of the federal government in education and schooling also appears to be changing. Several events show a trend toward a more visible, explicit role for the federal government in educational policy and program development. However, this does not mean increases in funding to schools or significant changes to service delivery at the local level.

One example of increased federal involvement in education is the "prosperity" agenda, which includes developing a significant policy paper on learning. The process involves a national consultation with several stakeholders in an attempt to determine common national goals in education. These are likely to be focussed on economic and vocational aspects of schooling. The Economic Council of Canada report, *A Lot to Learn*, is another example of federal involvement, as are the National Literacy Secretariat's federal-provincial agreements to fund several projects and programs in the provinces and territories.

Economic Downturn

Increased demands are being placed on school systems against a backdrop of economic restraint. Local school boards are being faced with the challenge of raising academic standards and maintaining services in the face of reduced financial contributions from provincial ministries of education, as a result of lower tax revenues. For example, the financially strapped province of Nova Scotia has limited education spending increases to 1 percent, leaving its 22 school boards with a projected \$20 million deficit. Local school boards such as Halifax/Dartmouth have responded by eliminating teaching positions, closing some schools, and severely curtailing "non-essential" programs, such as music and physical education.

Section 5. Conclusions

The Relevance of School Systems to New Reproductive Technologies

Many young Canadians are engaging in a variety of behaviours that, in addition to having consequences for their health and well-being in the short term, may jeopardize their reproductive health and ultimately their fertility. These behaviours include substance and alcohol abuse, poor nutritional habits, and sexual intercourse at an early age, with a number of partners, or with inadequate use of contraceptives.

In particular, unsafe sexual behaviours are placing adolescents at increased risk of contracting STDs. By Grade 11, almost half of young people have engaged in sexual intercourse at least once, and many are not using barrier methods of contraception for protection against STDs. The result of this adolescent sexual activity is a very high rate of STDs among

young men and women 15 to 19 years of age. Symptoms of these diseases are often not apparent, particularly in women, and therefore may go unnoticed and untreated for a long time. Ultimately, these diseases can result in infertility in a significant proportion of women.

If the current rate of STD infection among young women continues, the incidence of infertility in adult women is projected to increase significantly, with implications for the childbearing ability of the next generation as well as the need for new reproductive technologies in the future.

Based on these findings, there appears to be a very real need to change the knowledge and behaviours of young people with regard to their reproductive health. Preventive measures taken with adolescents now could reduce their potential need to rely on new reproductive technologies to bear children in the future.

School seems to be one of many places we should take on this challenge; the school system is where most young people are found at the time when they are most likely to face pressure to become sexually active or to engage in unhealthy behaviours as a means to increase their social acceptance.

Most schools are already involved in teaching reproductive health to students. The AIDS crisis has prompted provincial ministries of education and school boards to re-examine their policies and guidelines for sexuality education. From an early age, most children are now being taught about topics such as human reproduction, sexual abuse, pregnancy, contraception, and STDs.

So why are those involved in health promotion calling on schools to do more? Part of the reason is explained by the current health status of teens; STD rates indicate that existing programs are not as effective as they could be. There are a number of problems with the way in which sexuality education is being implemented:

- Some schools (the exact proportion is unknown) still do not offer any sexuality education, although it is mandated in all provinces.
- In high schools, too often sexuality education is offered only in junior grades. This means that the appropriate messages are not reinforced in senior grades, at the very time when many adolescents are most likely to feel pressure to become sexually active.
- Many reproductive health programs simply provide information to students and do not recognize the distinction between informing youths and actually changing their behaviour. Research has shown that awareness and knowledge about the issues do not necessarily translate to safe behaviour. Effective programs need to take into account the attitudes and social barriers that prevent youths from changing their behaviour.

 School programs are often offered in isolation from other elements such as health services, which could increase their impact.

Professionals involved in health promotion believe that a comprehensive approach to school health is more effective than providing health instruction as a single component. They maintain that health instruction should be integrated with "healthy" school services and environment (health clinics in schools to provide counselling and contraceptive services; condom dispensers in washrooms) and coordinated with community efforts and parental support. Some school boards have developed policies that favour such a comprehensive health promotion approach, but this is new and far from universal.

There is also an opportunity for schools to provide more information about genetics and reproductive technologies within human biology curricula, to assist individuals in making informed decisions about their reproductive options in the future. Science teachers are interested in covering health and social issues associated with human genetics, but they lack information and materials. As a result, these areas receive little or no coverage in science courses.

Religion and home economics courses in some provinces already cover new reproductive technologies and sexuality-related issues. However, as these are optional courses, there is less potential for them to have a real impact on the knowledge levels of most students.

A Realistic Role for Schools

The kinds of educational change required to prevent infertility among young people and to increase their knowledge about new reproductive technologies represent educational innovations rather than educational reforms, because, while they will involve some program changes, they will not substantially alter the way education is delivered. However, these potential changes must be viewed in the context of other demands currently being placed on school systems.

Schools are under pressure from an overwhelming number of societal concerns that are once again reorganizing the five basic functions of schooling. Strategically, it would be useful if the Commission could tie recommendations about reproductive health promotion and education about genetics and new reproductive technologies to existing curricula so that a significant increase in instructional time is not required.

Many school boards are being faced with the dual challenge of raising academic standards and maintaining existing services with reduced revenues. Some are responding by cutting "non-essential" programs, such as music and physical education. In financially strapped regions, convincing school boards to commit resources to improving their sexuality or family life programs may be difficult if basic services and programs are already under threat of being discontinued.

Calls for increased school involvement in health promotion and sexuality education mean that schools are being asked to play a role that families and community played in the past. Schools cannot take on the role of providing health services. These services need to be provided by health agencies. If schools are to provide more sexuality education, then parents, churches, and other community groups need to be involved to support their efforts. The comprehensive school health framework is one way to accomplish this objective. Some school boards have already developed policies that favour a comprehensive approach to school-based health promotion in responding to health and social problems affecting their students. There may be an opportunity to encourage other jurisdictions to move in this direction.

Implications for the Royal Commission on New Reproductive Technologies

In formulating its recommendations, the Commission may wish to consider ways in which schools could play a more active role in two areas: promoting adolescent reproductive health within sexuality education and providing information about genetics and new reproductive technologies in science curricula.

Specific suggestions for areas in which the Commission may want to recommend changes and some potential roles of key players who could help to implement the changes are outlined below. These suggestions are not meant to be comprehensive; they are meant to indicate some types of support different groups could provide for the educational innovations that are required.

Types of Educational Changes Required

Reproductive Health Education

The Commission may want to suggest that the challenge for school systems is to implement the curricula that have now been mandated by ministries of education. Where programs are in place, the Commission could suggest work to improve their quality, content, and duration.

Changes are most likely to be implemented if the efforts of schools are integrated with those of other groups and individuals, such as parents and health professionals, who have a vested interest in preventing infertility among youths. A collaborative approach that establishes partnerships between different levels of government, school system players, agencies, and community organizations will reduce the pressure on schools and create a greater momentum toward change.

Schools could improve the effectiveness of their reproductive health education in a number of ways. The Commission may want to suggest that schools take several actions:

- Extend sexuality education programs beyond Grades 9 and 10 to reinforce and build on students' learning about sexuality-related issues at the time when they are most likely to become sexually active.
- Re-examine the content and approach of existing sexuality education programs to determine how their effectiveness in producing the desired behaviours could be increased. Programs should recognize the difference between knowledge and behavioural change and encourage the teaching approaches that are most likely to result in the desired behaviour e.g., teaching communication skills, role playing.
- Increase the impact of school programs by adopting a comprehensive approach to school-based health promotion of sexuality education. This requirement would involve integrating school programs with other elements: accessible health services, parental involvement, and community support (e.g., churches, health professionals).

Science Curricula

Increasing young people's knowledge about new reproductive technologies can be accomplished by including new areas within science (biology) curricula. There is also an opportunity to incorporate units within home economics courses at junior levels, although student participation is probably not universal across all provinces.

Recommending a greater emphasis in science courses on reproductive technologies and the role of human genetics would link the Commission's goals to the call for an increased emphasis on core courses in general, including science. However, the objectives of those people wanting a greater stress on science for reasons of competitiveness may not be compatible with the prevention objectives of others. Proponents of prevention will need to develop the argument that "health is wealth" to sell the idea of providing a greater emphasis on reproductive health to some potential supporters of change. Economic arguments projecting the long-term costs to society of continuing high rates of STDs among youths would be persuasive.

A Potential Role for Some Key Players

This section outlines some potential roles for players who could help to improve the delivery of health/sexuality education. A discussion of how curriculum changes are implemented has been provided in Section 1 of this paper.

Increasing the effectiveness of sexuality education represents a much larger challenge than modifying science curricula, because it requires a collaborative approach between different groups and because ultimately the

objective of sexuality education is to change youths' attitudes and behaviour — a more difficult task than simply imparting knowledge.

Provincial Governments

Provincial governments can contribute in several ways. First, they can use an interministry approach to school-based health promotion. They can encourage interaction and collaborative efforts between those involved in education and those involved in the delivery of health care. Second, provincial governments can ensure the consistency of sexuality education programs between school boards, improving the quality of existing programs, increasing their duration, and improving the ability of teachers to teach reproductive health programs.

The CMEC might provide a forum for changes to be implemented on a nation-wide basis if the ministers could be convinced that the high prevalence of STDs among teens was an issue of national concern.

Specific provincial government actions might include the following measures:

- revising the health (or other relevant subject) curricula to make sexuality education, including coverage of STDs, mandatory in senior grades;
- mandating more extensive coverage of STDs, in addition to AIDS, at lower grade levels (7 to 9);
- providing funding and direction to school boards to aid in the development of specific programs, teaching materials, and teacher training for revised sexuality education programs. Provincial governments might provide models for effective sexuality education programs, including recommended teaching materials and parent information for school boards to use as is or modify if desired. Reducing the overall costs to school boards might be more likely to result in changes;
- encouraging school boards to adopt a comprehensive approach to school-based health promotion by providing funding and support for schools to integrate their efforts with local health departments, community groups, and others;
- increasing the level of training in sexuality education at teachers' colleges; and
- mandating the delivery of sexual health services in clinics in or near schools.

School Boards

School boards could increase the effectiveness of reproductive health programs in their jurisdiction through some of the following techniques:

 developing sexuality education programs, policies, and guidelines if they do not already exist;

- evaluating existing programs and revising them to increase the emphasis given to STDs, as well as improving their overall quality;
- providing teacher training;
- ensuring that materials are relevant and up-to-date;
- developing a policy recommending that schools in their jurisdiction adopt a comprehensive approach to school-based health promotion;
- authorizing and encouraging schools to refer students to health clinics;
- establishing interagency agreements with local health units to ensure cooperation on programs, policies, and services; and
- encouraging school principals to direct funds toward purchasing improved programs and materials for sexuality education.

School Principals and Teachers

School principals can encourage teachers to implement approved programs and seek additional training in teaching sexuality education. Teachers can advocate that their schools provide a greater emphasis on sexuality education and can solicit parental support for, and involvement in, the delivery of programs. Both can encourage parents to reinforce the messages learned in sexuality education in school by providing them with support materials.

Health and Social Service Agencies

Health and social service agencies can be funded by ministries of health to provide easily accessible information and counselling in or near schools and can conduct local community assessments of STD incidence. They can also provide in-service training for school district administrators and teachers.

Health Units

Health units can establish comprehensive policies on reproductive health and ensure that sexual health services are accessible to adolescents in or near schools.

Federal Government

The federal government in recent years has taken on a more visible and proactive role in educational policy and program development. Provincial ministries of education appear receptive to federal involvement in education as long as the process is cooperative. This political trend has positive implications for the way in which Commission recommendations suggesting a federal role in reproductive health education might be received and implemented.

The federal government can play a key role in collecting and disseminating information about the status of sexuality education programs in Canada. Specifically, it could be encouraged to

- fund research to update information about how many and which schools provide sexuality education and about program content and delivery;
- fund research into how to maximize the effectiveness of sexuality education;
- in conjunction with provincial ministries of education, develop objectives and guidelines for reproductive health programs and materials for use in schools; and
- fund national groups in education, health, and the community to allow them to collaborate with provincial governments and school boards in program development and implementation and provide clearinghouses for teaching materials.

National Groups

In education, these groups would include the national organizations representing ministry officials (Canadian Education Association), school superintendents (Canadian Association of School Administrators), school principals (Canadian Association of Principals), teachers (Candian Teachers' Federation), and parents (Canadian Home and School and Parent-Teacher Federation). In health, these groups would include public health officials (CPHA) and various special disciplines related to reproductive health. In the community, the sexuality organizations such as Planned Parenthood and broadly based coalitions such as the Canadian Association for School Health would be the best vehicles.

Appendix 1. List of Assessed Health Education/Sexuality Education Curricula

The following curriculum documents were reviewed for this project:

Prince Edward Island, Family Life Education (Draft), October 1988. Prince Edward Island, Health and Family Life Component (Draft), February 1988.

Prince Edward Island, Family Living 120, June 1989.

New Brunswick, Jr. High School, Human Growth and Development, 1988.

New Brunswick, Health and Physical Education: Addendum: AIDS, 1989.

New Brunswick, Jr. High School - Grade 9, AIDS Addendum, 1989.

Nova Scotia, Personal Development and Relationships (Draft).

Quebec, Formation personnelle et sociale, 1988.

Ontario, Family Studies: Intermediate and Senior Divisions and OAC, 1987.

Ontario, Physical and Health Education, Senior Division, 1975.

Ontario, Physical and Health Education, Intermediate Division, 1978.

Northwest Territories, School Health Program.

Northwest Territories, Family Life Education: AIDS Component.

Northwest Territories, Grade 7 Guide.

Northwest Territories, Grade 8 Guide.

Northwest Territories, Grade 9 Guide.

Manitoba, Family Life Education, 1990.

Manitoba, Family Studies 10-12, 1988.

Saskatchewan, Health Education: A Curriculum Guide; Division III, September 1985.

Alberta, Career Awareness and Life Management 20.

Alberta, Grades 7, 8, and 9 Guides.

British Columbia, Learning for Living: Primary to Graduation, Curriculum Guide, 1990.

Appendix 2. Results of an Informal Survey of Ministry of Education Officials

The following survey of ministry of education officials was done in the spring of 1991. Officials were contacted by telephone and asked to complete the attached questionnaire as it appears in this tabulation. Responses were then collated.

The initial contact in the ministry of education was the health education coordinator. He or she was asked to pass along the survey to relevant colleagues in the ministry of education.

	Not covered in mandatory program	_	Extensive coverage in mandatory program		Don't know
Instruction					
Grade 7					
Reproduction	1	2	7	2	0
Contraception	5	1	2	1	0
STDs	3	1	5	1	0
Infertility	6	4	0	0	0
Adoption	5	2	2	3	0
New reproductive technologies	8	1	0	0	0

Coverage of STDs, Infertility, New Reproductive Technologies (cont'd)

	Not covered in mandatory program	Some coverage in mandatory program	Extensive coverage in mandatory program	Covered in optional unit	Don't know
Instruction (cont'd	n				
Grade 8					
Reproduction	1	1	8	3	0
Contraception	4	3	2	2	0
STDs	2	2	3	2	0
Infertility	7	4	0	2	0
Adoption	5	5	0	1	0
New reproductive technologies	9	0	0	0	0
Grade 9					
Reproduction	1	1	8	2	0
Contraception	1	0	7	3	0
STDs	0	2	9	2	0
Infertility	5	5	0	0	0
Adoption	1	6	0	0	1
New reproductive technologies	8	1	0	0	1
Senior grades (10-12) Please indicate grade:					
Reproduction	0	4	3	2	1
Contraception	0	3	4	3	1
STDs	2	2	4	1	1
Infertility	2	4	1	3	1
Adoption	2	3	1	2	1
New reproductive technologies	3	2	0	3	2

Support Services

	Yes	No	Don't know	Other (please elaborate)
Are teachers authorized to refer students to health clinics for counselling for STDs, sexuality?	6	3	2	Informal, not officially authorized
Do health clinics provide counselling and information to adolescents re: STDs and sexuality?	9	0	0	Especially in urban centres
Are counselling and information services readily available to students?	7	4	0	Service is "slim"
Social support				
Does the sexuality/family life program include materials/information for parents?	8	4	0	
5. Do school boards have formal, written policies on sexuality/family life education?	5	2	3	Some, not all
Do school boards have community advisory committees on sexuality/family life education?	4	4	2	Some
Physical environment				
7. Do school boards allow condom dispensers in secondary schools?	4	4	0	Few, some schools

Science Education Programs

	Not covered in mandatory program	Some coverage in mandatory program	Extensive coverage in mandatory program	Covered in optional unit	Don't
Topics					
Human reproduction	3	3	2	1	0
Biotechnology	5	0	2	1	0
New reproductive technologies	7	0	0	1	0

Grade level:						
	Not covered	Some coverage	Extensive coverage	Don't know		
Topics						
Human reproduction	1	4	8	0		
Biotechnology	2	6	5	0		
New reproductive technologies	3	5	5	0		

Further Observations:		

FAMILY SCIENCES/HOME ECONOMICS EDUCATION

Junior High Compulsory Program (if applicable)

	Not covered in mandatory program		Extensive coverage in mandatory program	Covered in optional unit	Don't know
Topics					
Reproduction	5	-1	0	1	0
Contraception	5	0	0	1	0
STDs	5	0	0	1	0
Infertility	5	1	0	1	0
Adoption	3	2	0	1	0
New reproductive technologies	5	1	. 0	1	0
Senior					

Optional Courses

Grade level: ___

	Not covered	Some coverage	Extensive coverage	Don't know
Topics				
Reproduction	1	5	3	0
Contraception	2	3	4	0
STDs	2	1	4	0
Infertility	2	2	3	0
Adoption	2	3	3	0
New reproductive technologies	2	3	2	1

Further	
Observat	ions:

(Please complete for each course in this category)

Grade:	_			
	Not covered	Some coverage	Extensive coverage	Don't know
Human reproduction	2	0	1	0
Biotechnology	3	0	0	0
New reproductive technologies (human)	2	1	0	0
Further explanation	on:			

Grade:							
	Not covered	Some coverage	Extensive coverage	Don't know			
Human reproduction	0	0	2	0			
Biotechnology	1	0	0	0			
New reproductive technologies (human)	0	1	0	0			

Grade:				1
	Not covered	Some coverage	Extensive coverage	Don't know
Human reproduction	0	0	1	0
Biotechnology	0	0	0	0
New reproductive technologies (human)	0	0	0	0

Appendix 3. Summary of Research Findings on Health Education and Adolescents

		Speci	Specific Messages to Youth	outh		
	To reduce risk factors and enhance positive factors	Knowledge	Attitudes, beliefs, perceptions	Skills	Behaviours	Enabling/ reinforcing behaviours
About health	Be able to reduce risks, self-reinforce, relate well with parents and peers, and develop support networks (King et al. 1990).		Include messages about safe behaviours within other messages about avoiding health risks (Baldwin and Baldwin 1988; Belzer 1987).	Build skills in developing social networks, countering group norms (Fisher 1988).		
				Build decision- making skills (Croteau et al. 1981).		

	Enabling/ reinforcing Behaviours behaviours		Students • Sanction the should use of use of practise skills condoms by related to adolescents condom use, through social including norms. with partners, purchasing condoms, visiting clinics.	Teach explicitly about sexual limit setting,
	Skills Beh	Be able to formulate action plans (King et al. 1990).	Provide skills • Studen should society, practis, media, peer condor pressure to includit have sex negotie (Hacker with paper). 1989). purcha condor visiting	Teach social • Teach assertiveness explicitl skills (Millan about s and Ross limit set
Specific Messages to Youth	Attitudes, beliefs, perceptions	•	Messages should to eroticize the suse of condoms (Tanner and Pollack 1988).	Sensuality • Sensuality • Should be emphasized (Hacker 1989)
Specific	Knowledge		Message should teach the hierarchy of risk associated with different types of sexual activity and the advantages of postponement (Hacker 1989).	•
	To reduce risk factors and enhance positive factors		• Explicit messages should include limiting the number of sexual partners, using condoms and spermicides, and attending clinics for regular screening	(Solomon and DeJong 1989). Explicit messages should counter social norms
			About sexual health	

that sex is bad (Hacker 1989). maintaining

consistent with groups' norms behaviours so Fisher 1989). they appear adolescent preventive Reframe more

condom use, Provide skill condoms in discussions, negotiating introducing training in condoms, applying zes-erc partner male) cultural norms about (especially and social the use of should be smoopuos changed Kirscht Social

(Kelly et al. 1990; Schinke efuses to use assertiveness and exiting situations if the partner training in sexual condoms Provide 1984).

and problem solving for high-risk groups (Kelly et al. 1990; perceptions of (DiClemente adolescent adolescent **sehaviour** Change normal

MacDonald et

		Specific	Specific Messages to Youth	outh		
	To reduce risk factors and enhance positive factors	Knowledge	Attitudes, beliefs, perceptions	Skills	Behaviours	Enabling/ reinforcing behaviours
About STDs	Explicit messages should focus on risk behaviours (Lawrance et al. 1990).	Present STD information in an objective manner (Hanvey and Kinnon 1993).	Perceptions about risk need to be changed (Wober 1988).	Use walk- through and role playing (Fisher 1990a, 1990b).		
	Be able to self- reinforce, have positive relations with parents and peers.	Provide addresses and hours of clinics (Zabin et al. 1986).	Address the psychological influences about STDs (Lindeman 1988; Ross 1984).	• Analyze scenarios; buy, use, and dispose of condoms; evaluate STD infection (King et al. 1990).		
		arousing messages with suggestion for positive action (Solomon and DeJong 1986).	Reduce stigma; stress rights and responsibil- ities and positive behaviours,			
			especially regarding condom use			

 Define STDs, transmission, testing, symptoms, consequences, preventive behaviours, myths, responsibilities (King et al. 1990).

About new reproductive technologies

About family development About scientific aspects

About ethical aspects

About spiritual, religious aspects

	Enabling/ reinforcing behaviours				
	Behaviours				
- Inno	Skills				
openic messages in loan	Attitudes, beliefs, perceptions				
	Knowledge				
	To reduce risk factors and enhance positive factors				
		About social,	economic	aspects	About related issues

SIG	Programs, procedures, Legislation, services, policy practices support	Focus on Public attitudes and aconomic and acconomic acconomic acconomic and attitudes and social support factors (Danielson et acconomic and acconomic and social norms to women to (Danielson et acconomic and acconomic and social norms to women to (Danielson et acconomic and acconomic and social support factors (Danielson et acconomic and acconomic and acconomic and acconomic acconomic and acconomic acconomic and acconomic and acconomic and acconomic and acconomic acconomic and acconomic and acconomic acc
Specific Messages to Others	des, efs, otions Skills	Social support for adolescent use of condoms is required (Brown and Fritz 1988).
	Attitudes, beliefs, Knowledge perceptions	Dramatic • Social supplincrease in for adolesce infertility caused by condoms is STDs (Bowie et al. 1981; (Brown and Bryant 1990). Fritz 1988). Recognize that knowledge-only programs are not effective in changing behaviours (Baldwin and Baldwin and Baldwin 1988).
		Government policy makers

	Resources, support	education to those already infected to prevent re-infection (Cohen 1991).		
	Programs, procedures, services, practices	Set targets and guidelines for prevention (Hanvey and Kinnon 1993).	Use a comprehensive coordinated approach (Hanvey and Kinnon 1993).	Combine education with easy access to
Others	Legislation, policy	Develop national health goals re STDs, infertility (Hanvey and Kinnon 1993).	• Policies should address social, economic, and political factors, not just individuals (Aral and Holmes 1991).	Strengthen laws and regulations to
Specific Messages to Others	Skills			
Specifi	Attitudes, beliefs, perceptions			
	Knowledge	Recognize that STD programs should be based on principles learned from AIDS education.	Knowledge of guidelines for effective AIDS/STD education (U.S. Dept. Health and Human Services 1985, 1988).	
		•	•	

minors (Hume 1987). treatment for

1988).

Focus on risky behaviours in Policies and

prevention (Lawrance et al. 1990). support, and environmental changes (Nelkin 1987; Sisk et al. 1988). programs must be comprehen-sive, coordinated, and sustained. They must provide relevant education, services, social

		Specifi	Specific Messages to Others	thers		
	Knowledge	Attitudes, beliefs, perceptions	Skills	Legislation, policy	Programs, procedures, services, practices	Resources, support
					Prevention programs should combine	
					education with community resources, such	
					as hotlines, accessible	
					to condom purchases late at night (Zabin et al. 1986).	
					 Programs should build self-help/ 	
					advocacy groups and networks (Van Dam 1989).	
Institutions,	 Know national, 	Communicate	Be able to		• Focus	
agencies, decision	provincial/terri- torial, local	support for the program in the	manage opposition to	impact of education	programs on attitudes and	
makers	incidence rates	agency/	sex ed/STD	programs on	behaviours not	

(Mackie 1990).	Focus programs on young women (Hanvey and Kinnon 1993).	Focus on negative impact of gender and sex role inequalities (Hanvey and Kinnon 1993).
Kinnon 1993).	Education programs should provide information, foster social support, and provide means for people to change behaviour (Sisk et al. 1988).	messages about AIDS, STDs, and pregnancy prevention (Fisher 1990a, 1990b).
al. 1991).	Evaluate program effectiveness (CASA 1990).	•
	Define the target groups and program objectives clearly and realistically (CASA 1992a, 1992b).	Use marketing techniques to differentiate target audiences within the youth population (Canada, Health and Welfare Canada, 1991).

	Resources, support		
	Programs, procedures, services, practices	Work with variety of community organizations to deliver programs (Shaw 1988).	Use interagency approach (Soskolne and Robson 1989). Provide early detection and case-tracing
Others	Legislation, policy	Adequate inservice training for teachers, nurses, principals, counsellors, and administrators should accompany introduction of STD prevention programs.	•
Specific Messages to Others	Skills		
ahacı	Attitudes, beliefs, perceptions		
	Knowledge	Use marketing techniques to design programs (Campbell and Campbell 1990).	

Provide
 screening for
 adolescent
 women
 (Hughes et al.
 1989).

program focus

Include a

on sexual concept to improve contraceptive behaviours (Winter 1988).

Increase and improve professional training (Hanvey and Kinnon 1993).

Programs
 should address
 structural and
 psychological
 barriers to
 preventive
 behaviours.

		Specific	Specific Messages to Others	thers		
	Knowledge	Attitudes, beliefs, perceptions	Skills	Legislation, policy	Programs, procedures, services, practices	Resources, support
					• Focus programs on the combination of drug/alcohol use and sexual activity (Shaw 1988).	
					• Programs should also focus on high uses of drugs (Baldwin et al. 1990).	
					Take gender into account in programs.	
Professionals/ • practitioners	Be able to evaluate sex ed. programs (Neutens et al. 1991).	• Group targets • by their behaviours, not by risk groups (Salt et al. 1990).	Be able to assess feasibility of sex ed. program in communities.		• Shift focus on teen pregnancy to include STD prevention in communities (Fisher 1990a, 1990b).	
•	Know where to locate materials for	•	Be able to communicate effectively		Change practices in clinics, e.g.,	

(O'Reilly and Aral 1985).

programs (Neutens et al. 1991).

Be able to discuss sex adolescents.

Churches should offer education and counselling programs (Melton 1989).

Be able to develop programs with appropriate scope and sequence (CASA 1992a, 1992b).

Be able to exercise political skills in advocating programs (Haffner 1988).

organizations Community

Families Others Media

Appendix 4. A Comprehensive School Health Promotion Framework

Several national organizations in Canada (CASH, 1992a, 1992b) have defined a comprehensive approach to school-based health promotion as "a broad spectrum of program, activities and services which take place in schools and their surrounding communities."

That approach should be designed not only to affect individuals' health behaviours but also to change the environments in which young people live and learn. The programs, activities and services delivered within such comprehensive approaches are the responsibility of young people, families, professionals, institutions, agencies and organizations concerned with children and youth.

These individuals and organizations come from different sectors of society including education, health, social services, law enforcement, voluntary groups, business and labour, as well as governments at all levels.

Each of these contributors to a comprehensive approach can be involved in the delivery of instruction or support services, in creating a healthy physical environment within the school or in encouraging social support within the community or school itself.

Experience and research suggest that a comprehensive, integrated approach can influence the health-related knowledge, attitudes and behaviours of students. It should also be recognized that the primary determinants of health status, namely genetics, socio-economic status and various cultural and environmental factors, will limit the impact of school-based programs. This requires that realistic expectations for such programs be established from the outset. Shamai and Coambs (1992) show that unless society really wants change, schools will have a limited impact.

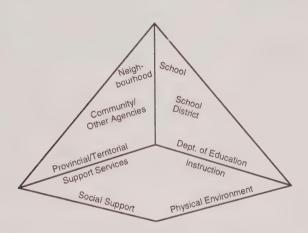
A comprehensive approach has four basic goals:

- to promote health and wellness
- to prevent disease, disorders and injury
- to assist children who are at risk
- to support the rehabilitation of children already experiencing poor health.

A comprehensive approach uses four basic means to achieve these goals:

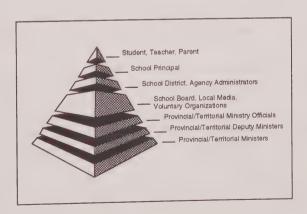
- instruction about health
- support services for children and families
- social support from families, peers, school staff and the community
- a healthy physical environment.

There are other models used to depict the holistic nature of effective school-based health promotion. Several member organizations of the Canadian Association for School Health have developed their own descriptions in consultation with other provincial organizations. Several organizations in the U.S. have endorsed an eight part model. The important thing is that the model is comprehensive and that it integrates the efforts of a variety of agencies.



Building The Pyramid

A pyramid illustrates the four basic components of the comprehensive school health framework; instruction, support services, physical environment and social support. It also shows that school-based programs depend upon policies, programs and funding from school boards and other agencies as well as from government departments.



Appendix 5. STD Prevention Program Recommendations

The following recommendations are listed to provide possible discussion points for the Commission with regard to developing and promoting a comprehensive approach to school-based prevention programs on infertility and new reproductive technologies (NRTs).

The recommendations are presented in two groups: short-term and long-term. The short-term recommendations are aimed at gathering the necessary information together, preparing for action at the national level, forming necessary partnerships, and deciding on basic strategies to guide a national prevention program, a part of which would use schools as a delivery vehicle.

The long-term recommendations suggest a strategy that works down through levels of administration: national, provincial/territorial, local community/school district, and local neighbourhoods/schools. The recommendations suggest how a national initiative on STD prevention might support action at those levels. Actions are suggested for the health, social service, and voluntary sectors on what they can do within school-based prevention programs.

In the Short Term

The following actions are suggested for the short term in order to develop a comprehensive approach to school-based responses to NRTs and the prevention of infertility.

A. Identify and establish necessary partnerships (one year)

The Commission should recommend that a collaborative approach be taken in health promotion and prevention strategies on infertility. Partnerships must include different levels of government, municipalities, school boards, other agencies, community organizations, the voluntary sector, and professions.

- 1. Health and Welfare Canada (HWC) should develop and deliver a comprehensive, integrated model for a national prevention program on infertility and sexual health promotion.
- 2. HWC should develop a mission (role) statement for schools concerning promotion of sexual health in consultation with educational authorities and organizations. This statement should recognize the limits of the school's influence on youth behaviours as well as its potential for success in developing specifically defined skills, attitudes, beliefs, perceptions, and behaviours related to infertility, STDs, and NRTs.
- 3. HWC should involve the mainstream educational leadership, as represented by the established education stakeholder organizations, in developing the national school-based prevention initiatives from the outset. This involvement should be achieved through surveys, focus

groups, formal and informal consultations, regular meetings with department of education officials, and direct contact with the deputy ministers of education.

Other organizations, representing the community and voluntary sectors, should also be involved in the development, promotion, and evaluation of the school-based prevention programs. However, the primary thrust should be to encourage the established groups within the school systems to modify and expand school-based prevention programs.

The mainstream leadership in health and social service organizations should implement the necessary school-related health and social services on STDs.

4. The federal government should openly use its resources and its constitutional capacity under its spending powers to develop and expand existing education programs to prevent infertility, STDs, and inappropriate uses of NRTs. This objective requires that the federal government establish a temporary, formal mechanism to facilitate intergovernmental cooperation. Models to be considered could include round-tables, joint federal-provincial committees, and the use of the already established liaison agreement between the CMEC and HWC.

B. Gather together necessary information and define specific targets

A national initiative to promote school-based responses to STDs must be based on current benchmark data and be focussed on clearly defined specific objectives.

- 5. The National Health Research and Development Program should fund a national study to describe current levels of adolescent knowledge, attitudes, beliefs, perceptions, skills, and behaviours related to reproductive health, including STDs. These data should include both quantitative data collected in a national survey and qualitative data obtained using focus group techniques. Analysis of these data should be used to develop a marketing approach.
- 6. HWC should conduct a survey of the knowledge, attitudes, beliefs, and perceptions of teachers, school administrators, parents, school nurses, medical officers of health, social workers, and social service administrators to determine if there are differences and, if so, how to best approach each category of personnel. This survey should be used to determine the best ways to communicate with these different categories of personnel. There are likely to be differences among the target audiences based on their professional assignment and where they live in Canada. These differences should be taken into account when planning social marketing/professional education campaigns.

- 7. HWC should fund national surveys of current sexuality education policies, programs, and practices of schools, school districts, health clinics, health units, social service agencies, and provincial and territorial departments of education, health, and social services to identify specific gaps and priorities for action.
- 8. HWC should prepare an inventory of exemplary school-based sexuality education programs to identify practical, effective models to be promoted in the national initiative.
- 9. HWC funding should be used to adopt an existing clearinghouse to serve as a resource for STD prevention materials for educators, health professionals, and social workers. This clearinghouse should be established in consultation with the target audiences it is to serve.
- 10. Education ministries should develop and define specific messages in curricula and programs that will speak effectively to youth about STD prevention.
- 11. HWC and national voluntary organizations should develop and define specific messages on STDs and reproductive health risks to inform government policy makers, institutional decision makers, professionals/practitioners, community organizations, families, and others.

C. Decide on frameworks for planning and action (one year)

A national initiative to promote school-based prevention programs must be planned and implemented within an established conceptual framework.

- 12. The powerful influences of social norms, economic conditions, and family values and practices should be recognized. Programs should alleviate or eliminate the negative influences that work against prevention programs.
- 13. A theory-based conceptual model for sexuality education (e.g., PRECEDE, Health Belief) should be used to plan prevention programs for STDs.
- 14. A comprehensive approach should be used that would include goals for sexual health promotion, STD prevention, intervention, and post-treatment support. The variety of means (instruction; health, guidance, and social services; social support; and a healthy physical environment in schools) to be used in such a comprehensive approach necessitates the involvement of schools, health and social service agencies, the community, media, and families. A comprehensive approach is not solely focussed on neighbourhood/school level actions but begins by promoting changes at community/school district and provincial/territorial levels.

- 15. This comprehensive approach should be adapted to include potential agency support and community involvement in science, home economics, ethics, religion, and social studies programs in schools.
- 16. School-based prevention programs should be only one delivery point for a larger initiative in STD/infertility prevention, which uses workplaces, colleges and universities, public and private broadcasting, youth organizations, family organizations, and places of worship for formal and informal education.
- 17. Education programs should be preceded by appropriate awareness and information campaigns.

D. Decide on basic strategies to be used in a national initiative (one year)

A national initiative to promote school-based prevention programs should use strategic opportunities currently available. The initiative should also be able to articulate its strategic thinking in order to overcome competition in reaching students in schools.

- 18. The federal government should emphasize helping leaders, administrators, and professionals at all levels to overcome their concerns related to school-based prevention programs; otherwise, curricula, programs, or videos that are produced may not be used. This approach would require that any educational materials produced in a national initiative be accompanied by a training program and consultants to facilitate implementation. Regular meetings with departments of education and health officials should be held as the initiative proceeds.
- 19. Federal departments should be instructed to begin the initiative by adopting internal, preparatory steps such as training staff, establishing general policies on health promotion in schools, and establishing interdepartmental and intradepartmental coordination mechanisms.
- 20. HWC should develop and support changes at the provincial/territorial level and at the community/school district level before the schools are expected to deliver effective programs.
- 21. A non-partisan, lobbying approach should be used to promote school-based prevention programs. This approach would recognize the politics of sexuality education, the specific decisions required from each of the players in the school systems, and the specific outcomes required from the many levels of educational decision making.
- 22. HWC should use a variety of approaches to initiate changes in Canada's two school systems, including the following:

- "top-down," through an agreement with the CMEC and bilateral agreements with provincial and territorial departments of education;
- "sideways," through joint projects and activities with the Canadian Education Association, Canadian Association of School Administrators, Canadian Association of Principals, and Canadian School Boards Association;
- "bottom-up," through joint projects with the Canadian Teachers' Federation and the associations representing guidance counsellors, school nurses, health education teachers, and home economics teachers; and
- "outside-in," through organizations such as the Canadian Association for School Health, Planned Parenthood, and others.

In the Long Term

The following long-term goals related to a national initiative to promote school-based prevention programs are described at the four necessary levels of involvement: national, provincial/territorial, community/school district, and neighbourhood/school.

A. Start at the national level

It is necessary that national goals be established in relation to the promotion of a school-based prevention program on infertility, STDs, and NRTs.

- 23. Federal research funding agencies, including SSHRC, NHRDP, and the Medical Research Council of Canada (MRC), should set aside targeted funds for research into the effectiveness of school-based STD prevention programs.
- 24. Existing interdepartmental coordinating bodies concerned with youth and children should be mandated to deal with STD prevention, or a new mechanism should be established.
- 25. Federal policy, programs, and procedures should place more emphasis on and funding in health promotion and school health promotion, including school-based STD prevention programs.
- 26. HWC should establish national adolescent health status objectives related to STDs.
- 27. Federal departments, especially HWC or Industry, Science and Technology, should be required to establish policies on school health and STD prevention and to develop appropriate implementation plans for such policies. These policies and plans should be developed in consultation with education, health, and social service authorities as well as non-governmental organizations.

B. Then approach the provinces and territories

As federal agencies and departments are redirected to respond to infertility, STDs, and NRTs, approaches to the provincial/territorial level should begin.

- 28. HWC should collaborate with the CMEC to undertake the following activities:
 - an informal consultation with provinces/territories using the Canadian Education Association;
 - the application of existing federal-CMEC agreements on educational materials, liaison with HWC, and international activities:
 - joint research activities; and
 - joint policy statements involving education ministers.
- 29. Federal officials should encourage provincial and territorial governments to develop the following:
 - a health promotion strategy for infertility prevention;
 - an interministry committee on STDs and NRTs (including representation from the ministry of education); and
 - an interministry policy and protocol on STDs/NRTs (including educational objectives).

This could be done by identifying exemplary models, evaluating such sample programs, regular liaison and communications with departmental officials, and project funding for national advocacy organizations that have provincial or territorial organizations capable of lobbying for such changes.

- 30. HWC should encourage provincial and territorial departments of education to
 - review and adapt existing curricula in health education/sexuality education, home economics, science, ethics, social studies, and religion;
 - develop guidelines/directives authorizing and encouraging student referrals to health clinics;
 - develop theory-based curriculum implementation plans on STDs;
 - promote departmental policies on sexuality education, especially as it relates to STDs.

This encouragement could be accomplished by identifying, evaluating, and disseminating exemplary models; establishing regular liaison with provincial/territorial department officials; organizing national skills and knowledge development workshops for provincial/territorial departmental

officials; creating target publications; and creating joint federal-department of education projects.

C. Emphasize community-based collaboration (five years)

School board officials, school district administrators, and their counterparts in health and social science agencies and in community-based organizations must be supported by HWC, through their provincial/territorial governments, in working together through school-based prevention programs in STDs and NRTs.

- 31. The Canadian School Boards Association should encourage school boards to
 - develop, implement, and evaluate comprehensive policies on STDs and sexuality education;
 - establish interagency agreements and activities with health and social service agencies; and
 - participate in community-based coalitions on STDs and infertility.
- 32. Ministries of education should identify, evaluate, and disseminate model materials, policies, agreements, or coalitions; train school leaders in workshops; and provide trainers and facilitators for each province or territory.
- 33. The Canadian Association of School Administrators should encourage school district administrators to
 - develop and implement theory-based programs in infertility education;
 - participate in community-based awareness campaigns;
 - publicize the value of their education programs; and
 - authorize school district employees to refer students to health clinics.

This encouragement can be provided by identifying, evaluating, and disseminating model programs; training school district administrators; providing consultants and facilitators to school districts; and disseminating resource materials.

- 34. Ministries of health and social services should support, fund, and encourage health and social service agencies to
 - provide easily accessible information and counselling services to or near schools;
 - conduct local community assessments of STD incidence; and

 provide in-service training for school district administrators and teachers.

Such encouragement can be provided by identifying, evaluating, and disseminating model programs; training agency staff; providing consultants and facilitators; and disseminating resource materials.

D. Maintain a focus on school/neighbourhood outcomes (seven to ten years)

The eventual impact at the school/neighbourhood level can be influenced by interventions directly aimed at schools but using national distribution systems and organizations representing the players at the school/neighbourhood level.

- 35. Faculties of education should make changes in all stages of preservice teacher training. This can be accomplished by identifying, evaluating, and disseminating model programs; organizing conferences; sponsoring articles in professional journals; and communicating directly with the deans of those faculties.
- 36. Professional associations representing teacher specialists in disciplines such as sexuality education; home economics; science; and ethics, moral, and religious education should offer teacher in-service programs on infertility, STDs, and NRTs.
- 37. The Canadian Association of Principals should develop and publish theory-based school implementation plans for education about STDs and NRTs.
- 38. The Canadian Home and School and Parent-Teacher Federation should encourage and offer effective parenting programs, including information about STDs. Programs for disadvantaged families should be a priority.
- 39. The Canadian Association for School Health should offer a compendium of model programs, materials, and strategies to involve employers, unions, places of worship, and voluntary organizations in STD prevention.

Notes

- 1. Dr. Carol Scurfield of Women's Health Clinic, testimony before the Royal Commission, 23 October 1990, Winnipeg.
- 2. Dr. Barbara Romanowski of the Expert Interdisciplinary Advisory Committee on Sexually Transmitted Diseases, Health and Welfare Canada, testimony before the Royal Commission, 26 November 1990, Vancouver.
- 3. The paper describes research that links a variety of factors, including poor nutrition, alcohol use, drug abuse, and tobacco use, to impaired fertility.

- 4. Terry Fallis of Planned Parenthood of Toronto, testimony before the Royal Commission, 19 November 1990, Toronto.
- 5. This study indicated that 50 percent of students who used the health clinic talked to their parents about human sexuality. See also King et al. (1988, 58). This study found that 47 percent of young Canadians prefer to obtain information about sex from their family.
- 6. Dr. William Bowie, Faculty of Medicine, University of British Columbia, speaking at the Royal Commission Colloquium on Prevention of Infertility, 22 October 1991, Ottawa
- 7. Ibid.

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Social Welfare and New Reproductive Technologies: An Overview

Sherri Torjman



Executive Summary

This paper explores how social welfare programs may increase or reduce the demand for new reproductive technologies (NRTs) and, conversely, identifies the areas where NRTs are likely to have an impact on the demand for social welfare programs and services.

The social welfare field may help reduce the demand for NRTs by preventing factors that cause infertility, in particular sexually transmitted diseases. In this respect, programs geared toward adolescents from unstable or abusive backgrounds, which provide social support and help prevent these youth from moving toward delinquent behaviour involving drugs, street life, crime, or prostitution, are significant. In addition, some jurisdictions sponsor family life education programs for students, parents, and professionals. Programs focussing on adolescent reproductive health are sporadic and largely underdeveloped.

Other programs in the social welfare field may increase the demand for NRTs. The very existence of social welfare programs and services — such as counselling, income assistance, child care, or homemaker services — may influence certain couples to use the technologies to have

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children. The possible link between the availability of child care services and the postponement of childbearing is of concern to the Commission in that a decision to postpone childbearing may contribute to fertility problems.

The paper also notes that the use of NRTs could have implications for the social welfare system and that, while the number of children born through NRTs may be small, their impact could be significant. The problems of these families may be complex, and they may present the system with new challenges, such as helping children deal with possible confusion related to multiple parentage. There are few precedents for

providing assistance in such situations.

The demand for income programs and social services that is directly attributable to NRTs cannot be precisely determined. The need will depend on factors unique to each family, including birth outcome, access to informal supports, and income level. Nonetheless, it is reasonable to assume an increased demand for certain services: those that support family care, such as counselling; those that supplement family care, such as income security programs, homemaker services, child care, and services for children with special needs; and those that substitute for family care, such as child protection services.

Introduction

This paper explores the links between social welfare and new reproductive technologies (NRTs). More specifically, this paper is intended

to accomplish two objectives.

The first objective is to help the Royal Commission on New Reproductive Technologies (the Commission) identify the components of the social welfare field that are likely to have an impact upon the demand for NRTs. The questions to be addressed are whether and how various social welfare programs increase or reduce this demand.

The second objective is to identify the areas in which NRTs are likely to have an impact upon the demand for social welfare programs and The questions to be addressed are whether and how the availability of NRTs and resulting birth outcomes are likely to affect social

welfare.

This paper is divided into two parts, each of which focusses upon one of the two objectives of the study. To achieve the overall task of linking social welfare and NRTs, some key concepts about social welfare — one of the most important, yet perhaps least understood, dimensions of Canadian society — are presented.

Only the basic concepts essential to understanding NRT-related issues are presented here. A more detailed discussion of social welfare is attached as the Appendix. Because this is an overview document, it cannot include much historical detail about the roots of social welfare and its evolution in this country. Readers are encouraged to consult the relevant literature to get a full picture of the breadth, scope, and diversity of the social welfare field.1

Key Concepts in Social Welfare

Social welfare addresses human well-being in its broadest sense. It is a generic term that encompasses "the network of legislation, social policies, programs, institutions, resources, and services that exist in modern society to ensure that all people have access to those things necessary to permit them to develop their potential as individuals in a manner acceptable to themselves, with due regard for the rights of others."²

In short, the term *social welfare* refers to a complex system of legislation, policies, programs, and services. Their purpose is to enhance the well-being of all members of society and to reduce social inequalities by

providing goods and services to persons in need.3

The social welfare umbrella covers several systems concerned with human well-being. These systems include income security, social services, housing, health care, education, and social justice. Generally, the term social welfare refers more narrowly to its principal elements: income security programs and social services. This paper focusses upon only the income security and social service dimensions of social welfare. Other dimensions, such as health care and education, are addressed in separate papers being prepared for the Commission.

While social services are sometimes considered synonymous with social welfare, they actually represent only one component of this broad field. Social services encompass a vast range of activities, including individual, marital, and family counselling; information and referral; child care; child welfare (child protection, foster care, and adoption); homemaker assistance; and respite care. Social services are delivered in a variety of settings, such as child and family agencies, schools, hospitals, community health and social services centres, and workplaces. Funding varies by type of service and the milieu in which it is delivered.

Social policies are guiding components of the social welfare system. More specifically, social policies articulate social goals and objectives — e.g., full employment, adequate income for seniors, or high-quality health care for all persons regardless of income. They provide direction for the specific income security programs and social services that subsequently

evolve.

Once governments have decided upon a social policy objective, they can translate this objective into action through two broad approaches. First, they can use taxes, transfers, or a combination of both to increase the income of some persons and reduce the income of others. This type of action helps equalize access to goods and services. Second, they can provide the services to which some people would be unable to gain access because of inadequate income. In Canada, as in other countries, social

policies have been effected through varying combinations of income transfers and social services.

Social work is another term sometimes considered to be synonymous with social welfare. Social work is the formal title for the profession whose aim is to restore or enhance the functioning of individuals, families, and communities. This goal is accomplished through counselling, group work, and work with communities such as designated urban neighbourhoods.

While social workers assume a key role in social welfare, particularly in the provision of services, they do not play an exclusive role. A wide range of professionals (and volunteers) are involved in social welfare programs and services, including physicians, economists, psychologists, teachers, child care workers, pastoral counsellors, and police officers.

The diversity of professional involvement is found primarily in the area of counselling, described more fully in Part 2. This diversity raises questions about standards for counselling services. With respect to social work in particular, all provinces except Ontario have acts that regulate the profession. However, legislated standards apply only to members who voluntarily join the professional association (except in New Brunswick and Prince Edward Island, where membership is compulsory).

There are some checks and balances in that social workers who practise in agencies are subject to peer review and ongoing supervision. Because there is less built-in scrutiny of social workers in private practice, most provinces now are considering the licensing of these professionals.

Another concern regarding social work practice is that most professional training focusses upon generic social work skills. While this training provides a solid foundation of counselling skills, it generally is not limited to a designated area of practice.

While graduate training tends to be more field-specific, training in highly specialized areas such as counselling around infertility, NRTs, or perinatal problems takes place primarily on the job. This means that the quality of services delivered depends largely upon the quality of training and supervision provided in the various work settings. Associations and informal networks have been formed in some specialized fields, such as perinatal social work, to establish practice guidelines.

Social workers who have been professionally trained at community colleges or universities generally carry out counselling, supervisory, and administrative functions. Some interventions also are carried out by individuals with diplomas or degrees in related fields, such as psychology, social science, educational counselling, pastoral counselling, or sociology.

Certain services, such as attendant care or homemaker assistance, are provided by persons who may lack formal professional training. They receive training from the service-providing agency and are supervised by professionally trained staff.

Key Players in Social Welfare

The main components of the social welfare system — income security programs and social services — are funded primarily through public dollars from various levels of government. However, the social welfare system has its roots in charitable activity undertaken primarily by voluntary and religious organizations. Through several centuries, social welfare has evolved from a charity-based mode to a mode supported largely, although not exclusively, by public dollars. This overview focusses only upon current roles.

Public Sector

Section 92 of the British North America Act of 1867 (subsequently amended and renamed the Constitution Act, 1982) establishes provincial authority over social welfare. The constitutional division of powers has had a profound impact upon the evolution of Canadian social welfare. Because provinces and territories have primary responsibility in this area, each jurisdiction has a unique system through which it provides social welfare programs and services.

Section 91 of the 1867 act assigned residual responsibility to the federal government for social welfare matters dealing with Indians and their land rights, immigration, veterans, and the management of penitentiaries. While its constitutionally defined mandate in social welfare is relatively narrow, the federal government nonetheless has assumed a key role. By virtue of its almost unlimited taxing and spending powers, the federal government administers and/or directly funds several major incomesupport programs. It also shares in the cost of health and social services.

More specifically, the federal government plays the following social welfare roles: (1) it provides funds directly to individuals through programs such as the Old Age Security pension; (2) it transfers funds to individuals directly and indirectly through the tax system; (3) it provides funds to organizations through granting programs such as National Welfare Grants for social welfare organizations and Grants to National Voluntary Health Organizations through the Department of National Health and Welfare; (4) it contributes to social services through cost-sharing arrangements under the Canada Assistance Plan (CAP) and transfers to health care under the Federal-Provincial Fiscal Arrangements and Federal Post-Secondary Education and Health Contributions Act (commonly referred to as EPF), described in the Appendix; (5) it funds employee assistance programs in federal departments; and (6) it supports services for populations such as status Indi ans and institutions such as penitentiaries for which it has constitutional responsibility.

As a result of federal responsibility for status Indians, social services for these persons are funded differently from the arrangements outlined in Parts 1 and 2. These services are supported primarily by the federal Department of Indian Affairs and Northern Development (DIAND) rather than through federal-provincial cost-sharing under CAP. Manitoba, for

example, has an extensive network of Native child and family services mandated under provincial law but supported through DIAND. The Department of National Health and Welfare provides health care services in the North.

Canada has been described as a 'bifurcated' welfare state because of the large, although not exclusive, federal role in income security coupled with the large, although not exclusive, provincial and territorial role in service provision.⁴ As indicated, provincial and territorial governments are responsible for the planning, development, implementation, and delivery of social assistance (commonly known as welfare) and social services.

Welfare is the income program of last resort. It comes into play when individuals have exhausted their personal resources. Assistance is provided to those who qualify on the basis of a needs test. The federal government, by contrast, provides financial benefits through demogrants (i.e., on a universal basis) or through an income test (i.e., based on level of income).

Provinces and territories may deliver services directly or may transfer funds to municipal governments or voluntary organizations to provide designated services. The availability of services varies not only by region but also within a province or territory. There usually are large disparities in service availability between urban and rural areas.

It is sometimes difficult to differentiate a health service from a social service. Some jurisdictions, such as Prince Edward Island, New Brunswick, Quebec, and the Yukon, have combined responsibility for health and social services within one ministry. In Quebec, for example, a variety of health and social services are delivered under the same roof through local community service centres (Centres locaux de services communautaires).

The involvement of municipal governments in social welfare is key in the "two-tier" provinces of Nova Scotia, Ontario, and Manitoba. In these provinces, provincial governments provide welfare for persons likely to be unemployed indefinitely, such as persons with severe disabilities; municipal governments grant welfare to persons likely to be unemployed for a short time, such as young, able-bodied persons. Municipalities in the two-tier provinces may provide certain social services as well. Provincial governments reimburse a portion of the costs.

Municipal governments also play an important role in promoting health and well-being by maintaining the urban infrastructure that forms the basis of a healthy environment, and by supporting public "goods" such as parks, recreational activities, cultural programs, and libraries.

Private Sector

In addition to public sector activity involving various levels of government, the private sector is involved in social welfare, especially in the provision of social services. The private sector includes the voluntary sector, the quasi-public sector, the commercial sector, and religious organizations.

The *voluntary sector* refers to agencies or organizations that provide social services such as counselling, group work, or homemaker assistance. Examples include family service agencies, Big Brothers or Big Sisters, the YM-YWCA, and community information centres. The voluntary sector had its roots in the personal interests of individuals, groups, and organizations. The child welfare movement, for example, can be traced to the concerns expressed by individuals over the exploitation of children.

Voluntary agencies range in size from small organizations staffed by volunteers to organizations with a large, professionally trained staff. These agencies generally are run by a board of directors elected by the members. Because the board and members set the direction of the organization, these are usually considered to have the potential for innovation and flexibility.

The primary weakness of voluntary agencies is the fact that they are constrained by lack of funds because they are supported by voluntary dollars — i.e., membership fees and community funds generated through United Way campaigns. Many voluntary agencies also receive government support through sustaining grants for their core operations and fee-forservice arrangements for services such as counselling or vocational training that governments purchase on behalf of persons in need.

Voluntary agencies in some communities are local branches of a provincial or territorial division that is affiliated with a national organization. For example, local branches of the Canadian Mental Health Association tie into their respective provincial and territorial divisions. The latter, in turn, link into a national organization. Voluntary organizations often are small and poorly funded; however, those that operate through a federated structure can represent a strong national voice through their extensive communication networks.

Organizations in the *quasi-public sector* combine the features of publicly supported and voluntary organizations. Their public component arises because they derive their mandate from legislative authority. They must conform to public standards and are supported by tax dollars. Yet, they are not strictly public organizations because they are run by a private board of directors. Many child welfare services not provided directly by provincial governments are delivered through quasi-public children's aid societies.

While the *commercial or proprietary sector* plays a small role in social welfare, its role has become more important over the past few years. Increasingly, governments have shifted responsibility for service delivery to the private sector. Commercial agencies operate in areas in which the public and voluntary sectors cannot meet the full demand and in which there is potential for profit. They have identified a market niche for child care, home care, and residential care for elderly persons. Commercial agencies are ineligible for cost-sharing under certain CAP provisions.

Religious organizations have had important direct and indirect influences upon the social welfare field. They have a long-standing involvement in protecting children, feeding the hungry, providing shelter for

homeless persons, and caring for the sick and elderly. In provinces such as Quebec, the Catholic church played a pivotal role in the early development of social services.

Religious organizations still provide a range of services. For example, the Salvation Army runs snowsuit exchanges, food banks, and shelters for homeless persons or young, single mothers. There are Catholic family service agencies and Jewish social services in many communities. (While Catholic or Jewish families are not obliged to seek services from these agencies, this option is available if they desire counselling within a religious context.) Religious organizations also have had an indirect impact upon social welfare by shaping values on abortion, sexuality education, and family planning.

Alternative Services

Traditional delivery of social services has been subject to increasing scrutiny and challenge over the years. Concerns include lack of service, restrictive eligibility criteria, and lack of input into service delivery. These concerns have spawned the development of alternative services which complement and, for some people, replace traditional social services.

The women's movement raised questions not only about traditional male/female roles but also about the extent to which traditional income programs and social services respond to women's needs.⁵ The movement has fuelled the growth of alternative women's services: information centres, rape crisis centres, transition homes for battered women, and counselling services supportive of alternative lifestyles such as lesbianism or childlessness.

With respect to childlessness, a recent study of Canadian families found there has been a slight shift away from parenthood as a central feature of family life. Couplehood is increasingly accepted as a valid form of family, although frequent references to these families as "childless couples" still can be found in the literature. In addition, more and more women are staying single and childless. In 1986, Statistics Canada estimated that 14 percent of Canadian women would never marry, up from about 10 percent in 1971. It is projected that 16 percent of the present generation may voluntarily forgo maternity, representing a considerable increase over the earlier peak from 1906 to 1911.

Despite the apparent growing acceptance of childlessness, married couples still are under pressure to have children. In a survey of voluntarily childless couples, all of the women reported feeling stigmatized by their decision not to have children. The author concluded that, to a certain extent, the stereotype of such couples as selfish, irresponsible, and abnormal still persists.¹⁰

The self-help movement represents another form of alternative service. It has grown dramatically over the past decade, with several hundred thousand members in Canada alone. Self-help groups have been organized around virtually every human problem, including infertility, drug

abuse, obesity, death, sexual abuse, and specific medical conditions. The primary purpose of these groups is to allow members to share their feelings and concerns around common problems.

Aboriginal people and ethnic minority groups have established services that are more culturally relevant and sensitive than traditional social services. The federal Secretary of State supports some of these services. For example, it allocates grants to Native Friendship Centres that provide a range of services to non-status Indians and Métis in urban centres.

Other Players

The Canadian Association of Social Workers is the national body representing the social work profession. It is linked to provincial and territorial divisions, each of which has a network of local branches. This body sets standards for professional social work practice in its code of ethics and seeks to influence social policy by developing positions on key social issues.

Organizations representing business and labour may provide social services such as child care or counselling in the form of employee assistance programs. They make financial contributions to voluntary social service organizations. They both represent strong, active lobbies that advocate changes to social policies and programs — often from opposing perspectives. 12

While social welfare is usually equated with formal programs and services, there is a large informal component to this field. Many families depend upon informal caregivers, such as friends, neighbours, or nannies, because they are unable to find or afford licensed child care. Most care for the sick and elderly is provided by informal caregivers — the spouses and children of these individuals.

The Diversity of Social Welfare

Clearly, the social welfare system encompasses a wide variety of programs and services directed toward different targets (e.g., children and women) for different purposes (e.g., provision of counselling, practical assistance, or income support).

In part, the diversity arises because the system must address so many facets of human well-being. Another factor is the system's residual nature (see the Appendix). Social welfare acts as the last resort system that "picks up" the problems, emotional consequences, and social costs generated by economic, technological, and social changes such as industrialization, unemployment, the labour force participation of women, and changes in family structure.

Because social welfare touches so many aspects of human well-being, it is best described as a "patchwork quilt" with many different pieces. The patchwork effect arises in part because many social services, such as counselling, are provided through voluntary organizations. Further, there is no statutory obligation for governments to fund many of the services,

such as homemaker assistance, that they do support. Because these services are discretionary, they are vulnerable in times of fiscal restraint. The primary exception is child welfare. All provinces and territories have in place a network of services that protect neglected or abused children.

The patchwork effect also arises due to the many players involved in the system. In any jurisdiction, governments, voluntary agencies, private businesses, and religious organizations are involved in varying combinations and assume different roles in service provision.

There is another important factor that explains the diversity of social welfare. Health care services are subject to a set of standards articulated in the Canada Health Act. These standards must be respected if provinces and territories are to receive federal financial transfers under EPF (see the Appendix).

Social welfare services are funded under CAP's cost-sharing provisions. In contrast to the Canada Health Act, CAP has few requirements tied to the transfers it makes to provinces and territories for welfare and social services. For example, while all jurisdictions must have in place an appeal mechanism whereby welfare recipients can question decisions made with respect to their individual cases, there are no specifications as to how these appeal systems should operate.

Trends in Social Welfare

The social welfare system must continually change in response to emerging needs and trends, such as the growth in the number of single-parent families. In addition to responding to trends, the system itself has been changing. This paper identifies those trends that are of direct interest to the Commission.

The trend toward privatization of service delivery, noted in the section "Key Players in Social Welfare," partly reflects government attempts to reduce deficits. In addition, there have been cuts to social service budgets in particular, especially in Ontario, Alberta, and British Columbia. These provinces recently have been subject to a federal cap on CAP (see the Appendix).

This factor has constrained many of the services that could potentially influence the demand for NRTs (e.g., services for street youth and the prevention of sexually transmitted diseases) or that could be required as a result of NRTs (e.g., counselling). The description of counselling in Part 2 explains how budget constraints have had an important impact upon social services and the type of clients they are able to assist.

Existing programs and methods of service delivery also have been subject to increasing scrutiny and challenge, particularly by the users of social services. In recent years, there has been unprecedented growth of the self-help movement and of alternative services such as women's groups. There has been a shift away from institutional services and residential facilities toward community-based care.

While these trends may not appear to be of direct interest to the Commission, they reflect important undercurrents. There has been a trend away from the professionalization of services (and especially the medicalization of services) toward more holistic forms of care and support. They reflect a desire for more direct consumer involvement in and control over decisions regarding health and personal needs. The growing acceptance of midwifery is just one example of these trends.

These undercurrents have evolved over several decades. Their roots can be traced to various movements concerned with civil rights, consumer rights, women's rights, and the rights of persons with disabilities as articulated by the independent living movement advocates. In Canada, the Canadian Charter of Rights and Freedoms has reinforced this new rights

consciousness and has empowered it with the clout of the law.

Trends away from the professionalization of services toward greater consumer control may be somewhat difficult to reconcile with NRTs. Research and practice in NRTs require extensive involvement of the medical and scientific communities.

In formulating its recommendations, the Commission must strike a balance between two potentially conflicting situations: the Commission should advocate conditions which ensure that NRTs are developed under the most rigorous of scientific standards and are used under the supervision of the most highly qualified and technically skilled professionals. At the same time, it must promote an environment that encourages consumer awareness and informed choice in decisions regarding the development and use of NRTs.

1. Aspects of the Social Welfare System that Relate to Use of NRTs

Does social welfare have an impact upon the demand for NRTs? Do NRTs have an impact upon social welfare? The simple answer to both questions is yes. Parts 1 and 2 explain in more detail the precise links between these systems.

Access to NRTs

A major purpose of social welfare is to redistribute social benefits to reduce inequalities. Thus, it is appropriate to examine how this purpose —

ensuring access to goods and services — applies to NRTs.

The current legislative framework plays a significant role in determining access to NRTs. The Canada Health Act defines *insured health care services* as medically necessary hospital services, medically required physicians' services, and surgical services that require a hospital for their proper performance. *Insured* means the costs of these services are covered

by medicare, the provincial and territorial health care system that receives federal contributions through the EPF funding arrangement.

If NRTs are defined as "medically necessary" services, then costs are covered through provincial and territorial health plans. They are provided as a service accessible to all Canadians. No user fees may be charged.

If provinces or territories decide that NRTs do not fall within the scope of a medically necessary service, these may be considered as a health care service to which user fees may apply. The implications for access to NRTs are obvious. Wealthier families would have access to these technologies while poorer families would not, unless there is in place a system of full or partial subsidy for families with incomes below designated levels.

Social Conditions

Social welfare may influence the demand for NRTs indirectly through general social conditions. Social policies generally seek to create an environment that promotes health and well-being through such means as adequate incomes, health care services, good quality housing, and protection from violence and abuse.

Efforts to improve social conditions may appear to be peripheral to the interests of the Commission. However, when viewed from the perspective of the link between good social conditions and overall well-being, these efforts are important in protecting the health of Canadians in general and their reproductive health in particular.

A recent report of the House of Commons Standing Committee on Health and Welfare, Social Affairs, Seniors and the Status of Women recommended that the federal government play a more active role in ensuring living conditions that promote a healthy environment and population. More specifically, the Committee recommended that "the federal government develop policies to make the nation healthy in those areas where it has jurisdiction under the Constitution, including the environment and areas that affect quality of life such as housing, income, employment, and post-secondary education."¹³

In addition to general conditions that promote health, good prenatal care in particular reduces negative pregnancy outcome in the form of low birthweight or infant mortality. Prenatal care includes both health and social services: regular physical examination; education on nutrition, exercise, and health habits; and adequate social support, such as financial assistance for dietary supplements or homemaker services, to help with other children in the family.

Reproductive Health

The social welfare field plays a preventive role through its efforts related to youth and reproductive health. There is a variety of social services geared toward adolescents from unstable or abusive backgrounds. The services provide social support and help prevent these youth from

moving toward delinquent behaviour involving drugs, street life, crime, or prostitution.

These efforts are important for reproductive health for two reasons. First, they help curb the spread of sexually transmitted diseases. Chlamydial infections, in particular, have increased fivefold since 1985, with the largest increase occurring among youth aged 15-19. Sexually transmitted diseases can cause complications that often result in infertility. Second, preventive efforts help reduce the risks of teenage pregnancy, generally associated with low birthweight, infant mortality, congenital defects, and developmental disabilities. 15

Most reproductive health services, such as providing information on healthy sexuality and family planning, dispensing birth control devices, and diagnosing and treating sexually transmitted diseases, are funded primarily by health dollars, — that is, provincial or territorial funds from general revenue sources bolstered by federal transfers under EPF. These services are delivered through public health departments, community clinics, or local branches of Planned Parenthood.

The Planned Parenthood Federation of Canada is a national organization that provides information on sexuality and dispenses birth control devices. It receives core funds from the National Voluntary Organizations Grants and Contributions Program. Branches receive funds from differing sources. In British Columbia, for example, the provincial government pays for the services on a fee-for-service basis through its medicare plan. By contrast, Manitoba affiliates receive \$500 000 in sustaining grants from the province.

Serena (Service de régulation des naissances) Canada is another national organization that receives core funds from the National Voluntary Organizations Grants and Contributions Program. It makes available information on natural family planning methods and trains "teachers" who provide counselling on fertility. These services are delivered in a variety of

settings, including community centres and hospitals.

Some jurisdictions also sponsor family life education programs for students, parents, and professionals. The purpose of the Family Life Education Program in Yukon, for example, is to promote healthy sexuality and relationships as well as to prevent unwanted pregnancy and the spread of sexually transmitted diseases. The Family Life Program in Prince Edward Island holds workshops for students and professionals on sexually transmitted diseases; it also organizes parent workshops on how to discuss sexuality with children.

While the negative consequences of exposure to sexually transmitted diseases and teenage pregnancy are well documented, programs focussed upon adolescent reproductive health are sporadic and largely underdeveloped. A recent report of the Federal/Provincial/Territorial Working Group on Adolescent Reproductive Health concludes that "sexual and reproductive health services across Canada are neither consistent nor universal. Only a few provinces have been active and innovative in

providing complete sexual health services." The report encourages governments to address the problem by establishing sexual health services, requiring sexual health education in school curricula, conducting research, and developing media campaigns to promote healthy sexuality.

The Working Group also noted the special problems among high-risk groups. "Access to and availability of STD and contraceptive services aimed at high-risk adolescent groups (such as school drop-outs, runaways, street

youth, prostitutes and drug abusers) is limited."17

Services directed toward high-risk youth are delivered primarily by voluntary social service organizations such as Boys and Girls Clubs, Big Brothers, and Big Sisters. While some agencies may receive government grants, they are supported primarily through memberships and local United Way dollars. There is also a large volunteer component to these services. The Big Brothers Association, for example, pairs adult male volunteers with boys from single-parent, mother-led families.

Other social services are geared toward youth already on the streets. They help these young people move off the streets and out of a lifestyle of drugs, crime, and prostitution. The services are delivered primarily by voluntary organizations such as the YM-YWCA, Youth Services Bureau, and alternative youth agencies, supported through combinations of government grants and voluntary dollars.

Government efforts also should be noted. The British Columbia government, for example, operates Reconnect, a program designed to help youth live healthier lifestyles and re-establish contact with their families. Services include individual casework, group work, and social/recreational

programming.

Some agencies direct their efforts toward youth by focussing upon the prevention of alcohol and drug abuse or upon the development of self-esteem. Provincial and territorial drug dependency commissions are largely, although not exclusively, responsible for drug prevention and treatment services in their respective jurisdictions. Provincial commissions, as well as local treatment and prevention services, are supported through health dollars.

In many communities, local branches of national voluntary organizations, such as the Canadian Public Health Association or the Canadian Mental Health Association, target programs toward adolescents in areas such as drug abuse, sexuality, and AIDS (acquired immunodeficiency syndrome) awareness.

Provinces also have an array of mental health services — both hospital- and community-based — that are geared toward assisting troubled youth involved in crime, street life, and prostitution. These are supported largely through provincial health dollars. Child welfare services also help neglected or abused youth. These services are supported through welfare dollars — i.e., provincial or territorial funds from general revenue sources bolstered by federal cost-sharing under CAP.

Efforts directed toward street youth are relevant to the work of the Commission. These services seek to remove young persons from lifestyles that put them at high risk of exposure to sexually transmitted diseases. Efforts to prevent the spread of these diseases and to reduce associated complications such as infertility may reduce the demand for costly reproductive technologies over the long term.

Despite the variety of interventions described here, efforts to address the problems of street youth generally are sporadic, disjointed, and chronically underfunded.

Information and Referral

People require information to make informed choices, yet the amount and quality of information about NRTs and other choices provided by social workers are likely highly variable. Despite the important influence that information and referral have upon the demand for NRTs, there is no way of monitoring these processes.

Adoption

Infertile couples may choose adoption instead of NRTs or may pursue adoption if NRTs have not produced positive results. There has been a significant drop in the number of children available for adoption. The decline is the result of several factors: increased use of birth control among young, unmarried women; easier access to abortion (although access is still a problem in most communities); the attempts by child welfare services to maintain children in their natural homes for as long as possible through family supports and removal of abusers; and the trend among young, unmarried mothers to raise their children rather than give them up for adoption.

With respect to the latter, in particular, only 10 percent of young, single mothers now choose to release their children for adoption. 18 Ontario figures show that, in 1974, nearly 90 percent of such mothers placed their children for adoption. 19 The U.S. figures are comparable. By the late 1970s, 90-95 percent of young, unmarried women chose to raise their babies on their own.20 This fact raises questions about the extent to which adoption is a realistic option for infertile couples. It may be necessary to re-examine international adoption procedures or to consider childlessness

as a more socially acceptable option.

Some people argue that services currently available to assist young, single mothers have encouraged many women to keep their babies rather than give them up for adoption. Voluntary agencies and religious organizations sponsor a range of special services for young, single mothers. The Salvation Army, for example, operates maternity homes in many communities.

Others argue that these services are not driving the trend toward adolescent parenthood; instead, they are responding to a real social need. Nova Scotia, New Brunswick, Manitoba, and British Columbia, for example, provide special services in recognition of the physical, psychological, social, and financial risks associated with adolescent pregnancy. Children of adolescents are at risk of poorer health and development. Adolescent mothers frequently drop out of school, experience chronic unemployment, and depend upon welfare for long periods.

Regardless of whether these services are viewed as driving or responding to the trend, the facts remain indisputable. Most single adolescent mothers now choose to keep and raise their babies.

The reduction in the numbers of children available for adoption also may be related to the trend in the child welfare field toward maintaining children in their natural homes. "Early child welfare services attempted to protect children through institutional placement as a way of separating them from homes perceived as hostile and depriving." Society now believes that it is best for children to grow up in their own homes; as a result, social workers put emphasis on keeping the child and family together whenever possible. There is a greater reliance upon services that support and supplement family care.

The conclusion that there is a relative lack of children available for adoption is valid if the problem is examined only within a national context. There may be many thousands of children who could be placed with families through international adoption. However, political, human rights, administrative, and attitudinal obstacles to international adoption make it a less feasible option than it might potentially be.

Social Supports

The very existence of social welfare programs and services may influence certain couples to have (additional) children. For example, services such as counselling, income assistance, child care, or homemaker services provide important supports that prospective parents may require before deciding to pursue NRTs. Without these services, they may believe that they lack the supports, such as family members or sufficient income, to raise a family.

It is difficult to document empirically the link between social supports and the demand for NRTs; however, a link can be assumed by virtue of normal decision-making processes. In determining a certain course of action, individuals generally weigh the positives and negatives in any given situation. In this case, supports such as income programs and social services are the positives that may encourage the pursuit of NRTs.

Personal testimony in relation to child care services appears to substantiate this link. The Task Force on Child Care was appointed by the federal government in 1984 to review the need for Canadian child care services.

The Task Force received letters from many women who noted that the lack of child care services had influenced their childbearing decisions. In

some cases, women had chosen not to have children or to have fewer children because they had no access to high-quality, affordable child care. In other cases, women had decided to postpone their childbearing until they had saved enough money to purchase private care or until better community services were in place. The following letter to the Task Force illustrates the point:

I ask you to take a look at the question of how many women are choosing not to have children because there is no system of child care in this country to replace the extended family network which no longer exists. How many other women like me are there, who are educated, responsible and caring, but who know that having a child may not be possible until there is some assurance that a system exists to ensure that it is looked after while its female parent works?²⁵

The possible link between the availability of child care services and the postponement of childbearing is of concern to the Commission in that the decision to postpone childbearing may contribute to fertility problems. A recent study of Canadian families notes that: "Delayed childbearing tends to reduce a woman's chances of having children, for both biological and social reasons. Fecundity drops in the thirties, and couples may find themselves involuntarily childless, or sterile." 26

2. Implications for the Social Welfare System from Use of NRTs

This discussion considers only the income security and social service dimensions of social welfare. More specifically, it focusses upon income programs and social services directed toward families and children. Before examining the specific programs or services that may be affected, it is

important to consider the relevant context.

There are no firm Canadian data or standard national procedures for collecting information on the numbers of babies born through assisted conception methods. However, it can be assumed that, in relation to the total number of Canadian births, the numbers are small. The use of NRTs is not widespread. Further, only Ontario currently classifies the procedures as "medically necessary" and thereby assumes their full costs under the provincial health plan. A British study notes that, despite the rising numbers of higher-order multiple births (i.e., triplets, quadruplets, quintuplets, and sextuplets), these births remain rare. ²⁷

In short, the potential impact of NRTs upon the social welfare system is likely to be small if considered only in a quantitative context. Yet, this conclusion must be tempered by two factors. First, use of these technologies might increase if NRTs become classified as "medically

necessary" services whose costs are insured by all provincial or territorial health plans.

Second, while the impact of NRTs upon the social welfare system might be small in a quantitative sense, the impact may be significant in a qualitative sense. While there may be few people who require service, their problems may be complex. These people may present the system with new challenges, such as helping children deal with possible confusion related to multiple parentage. There are few precedents for providing assistance in such situations. Counselling for problems arising from prenatal diagnosis (PND) or NRT procedures also may involve new knowledge or skills for which training may be required.

The British study of triplets and higher-order births confirms this qualitative "burden":

Furthermore, since these births are rare, there are few professionals or parents from whose experience others can draw. Only a small minority of health visitors or general practitioners will ever encounter triplets or quadruplets. Even neo-natal paediatricians, who specialise in the hospital care of preterm babies, may not see a triplet or higher order multiple birth every year. Consequently, public knowledge about these children and the problems they may pose is limited. Apart from mutual support between parents, the information and support available to parents and professionals may be far less than that expected or needed.²⁸

There is no conclusive research specifically linking NRTs with designated income programs and social services. But it is not unreasonable to infer an increased demand for certain programs and services in response to the stresses involved in many NRT procedures.

For example, there likely will be a greater need for counselling services as a result of PND as well as some procedures involving assisted conception (e.g., in vitro fertilization [IVF]). Certain NRT procedures may result in multiple births and associated low birthweight. These may generate demand for more early intervention services to offset developmental delay.

The impact may be more long-term than the immediate post-natal period. For some but certainly not all children, low birthweight has been linked with learning disabilities and other developmental delays that may not become apparent until school entry.

At the same time, however, there may be a reduced demand for services for children with special needs. Some parents who have been informed of a serious condition or abnormality through PND may make a difficult choice and decide to terminate the pregnancy. Another possibility is that certain anomalies may be correctable through fetal surgery.

Families also may require special services and concrete assistance. The need for financial aid, such as the Child Tax Benefit, is unpredictable; it will be determined by family income.

Many families will require some form of social service to help them cope with the emotional and physical stresses associated with multiple

birth. The precise need for services, such as homemaker assistance or child care, will depend upon the type and extent of informal supports available to families. For example, grandparents, other relatives, friends, and neighbours may provide regular or occasional child care. The demand for these services also will depend upon families' ability to purchase assistance privately.

In the absence of informal supports and social services, these stresses may create the conditions for abuse. There could be an increased need for

child welfare services.

In short, the demand for income programs and social services that is directly attributable to NRTs cannot be precisely determined. The need will depend upon factors unique to each family, including birth outcome, access to informal supports, and income level. Nonetheless, it is reasonable to assume an increased (albeit relatively low) demand for certain services: counselling, early intervention services to offset developmental delay, child benefits for some families, and, to a certain extent, homemaker services and child care.

The social welfare programs and services that may be affected by NRTs may be categorized as those that support family care, those that supplement family care, and those that substitute for family care.²⁹

Services That Support Family Care

Counselling Services

Counselling is the primary support service of interest to the Commission. The purpose of counselling services is to provide support to persons under stress and to restore their psychosocial functioning. Counselling may involve individuals, couples, families, or small groups experiencing similar problems. NRT-related counselling may be available through health care facilities, family service agencies, private practitioners, and employee assistance programs (EAPs).

Generally, counselling services are provided by social workers. These services include crisis intervention, grief counselling, individual therapy, marriage counselling, and emotional support. In addition to or in place of formal services, some individuals may seek help through alternative services, such as women's centres, self-help groups, and informal networks.

Whether individuals seek formal and/or alternative sources of assistance, NRTs will generate a need for counselling and support at several points. PND likely will create a need for counselling whenever parents are faced with the prospect of a negative birth outcome. Those who have sought some form of assisted conception may require counselling throughout the NRT protocol at the prenatal, perinatal, and post-natal stages and on a long-term basis. There also may be a need for counselling and support even at the pre-NRT phase, that is, on diagnosis of infertility. Both men and women experience intense emotional reactions to

Both men and women experience interise chrotional reactions to infertility, including emotional pain and suffering, depression, anger,

anxiety, guilt, concerns about bodily functioning and reproductive competence, confusion, desperation, hurt, fear, embarrassment, humiliation, symptoms of crisis, and loss of control, self-confidence, and self-esteem.³⁰ Many couples experience feelings similar to the stages of grief. They grieve over the pregnancy they may never have, the children they may never bear, the parenting role they may never play, and the loss of genetic continuity.³¹

Counselling services may be needed if infertile couples decide to adopt a child or as they attempt to come to terms with the possibility of childlessness. Counselling also may be required if infertile couples decide to proceed with some form of NRT. Procedures such as IVF or gamete intrafallopian transfer (GIFT) are complex therapies consisting of several steps, with a chance for failure at each step. Patients oscillate between feelings of euphoria and despair depending on the success of each phase.³²

Studies of NRTs note that these technologies generate high levels of stress. A U.S. study of 200 couples seen at an IVF pre-treatment consultation found most had normal psychological profiles before the treatment. The treatment itself, however, generated significant levels of

anxiety and depression.33

A study of couples receiving IVF treatment in New Zealand found that only eight percent of respondents had received counselling in connection with infertility. Couples would have liked counselling throughout the entire process. The desire for counselling ranged from 32 percent while considering IVF, 39 percent if not accepted, 58 percent while undergoing treatment, to 60 percent if the treatment was unsuccessful.³⁴ Comparable Canadian data on satisfaction with IVF procedures are unavailable.

Provision of information about the procedures is an important component of the counselling process. Often, couples must absorb an overwhelming amount of medical information while undergoing infertility treatment. A study of satisfaction with IVF procedures found that 60 percent of women were not fully satisfied with the opportunities for

asking questions and for discussion during the treatment. 35

Counselling also may be provided through groups (some operate on a self-help basis without professional involvement). Such groups help individuals restore self-esteem, increase their knowledge of alternatives, reduce isolation, and discuss fears such as losing one's spouse or the possibility of living without children. "Universalization is reassuring, and the opportunity to meet other couples in the same situation can often provide a sustaining support. For many, support groups for infertile couples serve this purpose well." 36

Support also may be provided throughout treatment by means of innovative approaches, such as stress management programs. The Northern Nevada Fertility Clinic, for example, has developed a special

relaxation tape that it provides to prospective patients.³⁷

In addition, there may be a need for counselling in the case of a successful NRT result or when a particular health condition is detected

through PND. Social workers assigned to the neonatology or obstetrics service in hospitals provide counselling around the emotional consequences of high-risk medical situations.

Social workers also arrange practical assistance where required. For example, pregnant women frequently are admitted to hospital at the prenatal stage for pregnancy-related complications or confirmation of fetal abnormalities. Prospective parents may need to grapple with difficult decisions upon discovery or confirmation through PND of a serious problem. Social workers may help parents who decide to proceed with the pregnancy cope with the fear, anxiety, anger, and guilt that are common responses to uncertain birth outcomes.

Counselling may be required to help families handle the emotional impact of learning after the birth about a life-threatening illness, syndrome, or chronic condition. In the event of prolonged hospitalization, social workers may arrange practical assistance, such as child care or homemaker services.³⁸

Assisted conception also may generate a need for counselling and support months or even years after the post-natal period. Couples may experience stress and marital strain arising from the demands of multiple births or from the loss of one or more fertilized embryos. Children confused by or concerned about their biological parentage may seek assistance.

Counselling for NRT-related difficulties may be provided in one of four settings. First, counselling may be offered in a hospital or health care setting such as a community health clinic. Costs would be covered through provincial or territorial health dollars with a federal contribution through EPF. There is no charge to the user if the counselling is considered to be part of the health care services — e.g., helping parents cope with the predicted outcomes of PND. Similarly, counselling associated with infertility is covered as a health care cost if it is provided as part of a hospital or medical service.

However, certain NRT procedures are not defined as "medically necessary." In this case, user fees may be charged for the NRT procedures and associated counselling. The fact that these services are not considered "medically necessary" does not automatically mean that user fees will be levied.

Most provinces provide home health care defined within the Canada Health Act as an "extended health care service." Several provinces do not impose user fees because the individuals for whom these services are intended — persons with disabilities and the elderly — generally are unable to afford the costs. Nonetheless, provinces or territories may charge for such services without penalty or loss of federal transfers under EPF.

Second, persons seeking help in relation to infertility or an NRT-related problem may seek assistance from a family counselling agency. They may prefer to consider their options outside the medical milieu, or they may seek counselling within the context of their religious values.

Most family counselling agencies are voluntary organizations whose funds are derived from a number of sources, including the United Way, donations, and fees. Clients must pay for counselling services provided by family counselling agencies. They pay on the basis of a sliding fee scale that generally takes into account both their level of income and family size. While counselling costs vary throughout the country, the national average unit cost for counselling is \$80 per billable hour, which includes agency overhead costs.³⁹

Persons who cannot afford the service may be eligible for full or partial subsidy. In most cases, those who qualify for subsidy are welfare recipients. This limitation arises from the intricacies of CAP cost-sharing arrangements.

For agencies to qualify for cost-sharing in respect of fee-for-service arrangements, they must provide the designated service to persons who qualify on the basis of a needs test that considers level of need, assets, and income. This is the test used to determine eligibility for welfare assistance.

Under the CAP assistance provisions, agencies provide the services and bill the provincial government (or sometimes the municipality in provinces with two-tier welfare systems). The government is then reimbursed for 50 percent of the costs under CAP. Under the CAP welfare services provisions, by contrast, agencies may receive money that offsets some of the costs incurred on behalf of persons who qualify on the basis of an income test.

The net result of this funding arrangement is that subsidies are available primarily for low-income families. Despite the availability of subsidies, agencies do not have access to unlimited funds. The director of a local family service agency in Ontario, for example, explained that the organization may tap into a pool of subsidy money worth about \$127 000 per year. The funds are intended to subsidize counselling services for low-income families. This amount is generally spent by June of any given year; the agency must then find ways to offset the shortfall. Further, some municipalities do not provide any subsidy money for counselling services, which are considered to be a discretionary expenditure.

Family counselling agencies may decide to refer some clients to other counselling services supported through a different funding arrangement. For example, a couple seeking NRT-related information or assistance may be referred to a local health clinic. The clinic is more likely than a family counselling agency to have the expertise to deal with an NRT-related problem, and the costs of counselling would be covered as a health-related service.

Individuals and couples experiencing fertility problems or emotional difficulties associated with uncertain birth outcomes may also seek counselling from social workers or other private practitioners. In this case, the clients are solely responsible for the fees charged.

Individuals may seek available counselling through an EAP at their workplace. This service is funded by employers; the federal government

supports EAPs in federal departments. In most cases, however, EAP counsellors do not provide ongoing counselling services — especially if the problem is related to a highly specialized area such as PND, infertility, or methods of assisted conception. The primary role of the EAP counsellor is to refer individuals to the appropriate counselling resources. In this case, a referral would be made to a health care facility, family service agency, or private practitioner.

Services That Supplement Family Care

There are four major types of programs and services that supplement family care: income security programs, homemaker services, child care, and services for children with special needs. Their purpose is to bolster the care provided by the natural family through various forms of concrete assistance.

Income Security Programs

This section focusses only upon child-related income programs. Benefits paid on behalf of children fulfil several purposes.⁴⁰ They recognize parenting as an important social role and reward this activity through financial compensation. They promote horizontal equity by recognizing and compensating for the heavier financial burdens carried by families with children. Child benefits play an anti-poverty role by assisting low-income families. Finally, these benefits create an economic stimulus by providing families with additional resources to purchase goods and services.

Financial benefits are provided directly to individuals through a transfer of cash from government to recipient, or they are delivered via the tax system by offsetting certain costs such as child care. In the area of income security, it is difficult to predict the extent to which program costs will increase as a result of NRTs. Eligibility for the Child Tax Benefit depends upon net income. Families with incomes that fall below a certain level are eligible for benefits; families with net incomes above the designated level do not qualify for assistance.

Eligibility for welfare (or social assistance) is even more rigorous. Applicants must qualify on the basis of net income, the value of their assets, and their basic and special needs. The extent to which the demand for these programs will increase as a result of NRTs will depend upon the family's financial and social circumstances.

Direct Transfers

Child Tax Benefit

The new federal Child Tax Benefit came into effect in January 1993. It combined three former programs that provided financial assistance to families with children — family allowances, the refundable child tax credit. and the non-refundable child tax credit. The Child Tax Benefit has two components: a basic component and an earned-income supplement.

In 1993, the maximum annual payment under the basic component is \$1 020 for each child aged 7 to 17. Children aged six and under are eligible for a maximum of \$1 233. The third and each subsequent child in a family receives an extra \$75 a year. Benefits are delivered through monthly cheques — like the former family allowances.

Families with net incomes of up to \$25 921 in 1993 receive the maximum benefit. Above that income level, payments are reduced by 5 percent for families with two or more children (i.e., by five cents for every dollar above the income limit) and by 2.5 percent for families with only one child. The cut-off or disappearing point for a family with one child, or two children under age seven, is \$75 241; for a family with one child under age seven and one child between the ages of 7 and 17, it is \$70 981; and for a family with one child or two children between the ages of 7 and 17, it is \$66 721.

The second component of the Child Tax Benefit is the earned-income supplement, which helps working-poor families with employment incomes of \$3 750 or more. Over this base level of employment earnings, the supplement phases in at a rate of 8 percent. The maximum annual benefit begins once family earnings reach \$10 000 and continues until net family income reaches \$20 921.

Above the \$20 921 income level, the earned-income supplement is reduced by 10 percent of net family income. It disappears when this income reaches \$25 921. The supplement is included in monthly cheques.

The Child Tax Benefit is only partially indexed — to the amount that inflation exceeds 3 percent a year.⁴¹

Unemployment Insurance

Maternity benefits under the Unemployment Insurance Act provide income for mothers who take leave from work at the time of childbirth. Beneficiaries are entitled to 60 percent of the average of their last 20 weeks of insurable earnings in the preceding 52 weeks, to a maximum of \$408 per week in 1991. Benefits are provided for a 15-week period around the birth.

Mothers and/or fathers are eligible for an additional 10 weeks of parental benefits; this 10-week provision applies to adoptive parents as well. Five extra weeks are permitted for either parent of children who are aged six months or over when they leave hospital if these children have health-related problems. The benefits also can be shared by parents.

These benefits are provided through an insurance-based arrangement supported by employer and employee contributions. Only persons who have made the required contributions are eligible for benefits. Thus, parental benefits will increase as a result of NRTs only if parents have worked the designated number of weeks and made the required contributions.

Provincial Child Benefits

Quebec, Manitoba, and Saskatchewan provide financial assistance to families on an income-tested basis; that is, families qualify for assistance if their net incomes fall below designated levels.

The Parental Wage Assistance Program in Quebec (Aide aux parents pour leur revenu du travail) grants assistance that varies by level of income, number of children, child care costs, and housing costs. Under the Child-Related Income Support Program, Manitoba provides \$30 a month per child to families with net incomes of \$12 384 or less. Under the Family Income Program, Saskatchewan grants \$100 a month for each of the first three children and \$90 for the fourth and subsequent children to families with net incomes at or below \$8 700 plus the annual value of (the former) family allowances.

Welfare

Welfare is Canada's major needs-tested program. The needs test takes into account three factors: the value of applicants' liquid and fixed assets; their basic and special needs; and the resources, including income from employment, pensions, and government transfers, available to meet these needs.

While welfare often is referred to as a single program, there actually are 12 welfare programs in Canada — one in every province and territory. More precisely, there are hundreds of welfare programs, considering the two-tier welfare systems in the provinces of Nova Scotia, Ontario, and Manitoba.

Under two-tier systems, provincial governments are responsible for providing benefits to persons likely to be unemployed for extended periods. Municipal governments in those provinces grant assistance to persons likely to be unemployed for shorter periods. Ontario municipalities must follow a provincial standard for rates. By contrast, the 66 municipalities in Nova Scotia and the 202 municipalities in Manitoba set their own rates.

Welfare is a program of last resort. It provides financial assistance to persons who have exhausted their personal resources or whose needs exceed their available resources. Benefits for basic needs such as food, clothing, and shelter are low; they fall well below the poverty line in all parts of the country. Basic allowances may be supplemented by special assistance on a discretionary basis. Welfare workers determine who qualifies and how much extra assistance will be granted.

Each province and territory has a list of the goods and services that it funds as special assistance. These generally include assistance for health-related and work-related needs. All jurisdictions except New Brunswick provide extra monthly amounts for pregnant and lactating women. Ontario and British Columbia grant extra benefits for multiple births

Indirect Transfers

Equivalent-to-Married Credit

Single parents are provided special tax assistance. They can claim a larger amount for the first child through the equivalent-to-married credit worth \$895 in 1991 or \$1 387 if average provincial tax credits are included.

Child Care Expense Deduction

The federal government provides indirect assistance to offset child care costs through the child care expense deduction. In 1993, the deduction was worth \$5 000 per child aged six or under for whom child care receipts were available. The maximum deduction was \$3 000 for children aged 7 to 14.

Homemaker Services

Homemaker services refer to practical assistance for parenting or household management. The need for homemaker services may arise from stressful circumstances such as illness or prolonged hospitalization of a parent. These services also may be required for persons overwhelmed by their parenting responsibilities, as might be the case in multiple birth.

A British study of families with triplets and higher-order births described the difficulties they experienced arising from "the sheer exhaustion, the weight of the responsibility for three, four or more children of the same age and the difficulty of getting out with them in comfort and safety. Access to people and to places outside the home may be restricted, or quite literally prevented, particularly if there is no regular helper available."⁴³

While provincial governments generally set standards for homemaker services, their delivery varies widely. In some cases, these services are provided by provincial governments, municipal social service departments, or voluntary agencies such as the Visiting Homemakers Association. Families that can afford the costs may purchase these services privately from commercial agencies.

As with most social services, funding is a function of delivery. In general, homemaker services are supported through varying combinations of client fees charged on a sliding scale, voluntary dollars raised through local United Way campaigns, provincial dollars in certain provinces, and federal contributions under CAP. Federal dollars may be transferred under either the assistance or welfare services provisions of CAP, depending upon whether needs or income tests are used to determine eligibility for subsidy.

There likely will be an increased need for homemaker assistance as a result of NRTs. The sheer physical demands involved in infant and child care, especially in the case of multiple births, will generate pressures for homemaker assistance. However, the precise extent of the demand is difficult to ascertain.

Some families may have informal supports, such as grandparents and other family members, who can provide respite and extra assistance. Other

families may be able to purchase privately the services of a housekeeper or nanny with no apparent impact upon the formal social welfare system. The pressure on the publicly funded social welfare system depends upon families' access to personal and private resources. With respect to the latter, in particular, there likely will be few low-income families who use NRTs if access continues to be restricted through the imposition of user fees (as in all provinces except Ontario).

Child Care

Child care services supplement parental care for part of the day, generally while parents work. Child care services also may be used as a child protective service to reduce the amount of time a child spends in a stressful home environment. These services are geared primarily toward preschool children, although there are after-school programs for older children.

Child care services are organized differently in every province and territory. In general, the two major categories of care are licensed and unlicensed child care.

Licensed child care refers to services regulated by the provincial or territorial government in areas such as health and safety, child/staff ratio, and space requirements. Licensed services are generally provided in day-care centres that look after groups of children. Day-care centres operate under various auspices, including local governments, voluntary and religious organizations, commercial operations, and, increasingly, work settings such as hospitals and government departments. Licensed child care also may be provided in family day-care homes in which caregivers look after a small number of children in their own home.

Families that cannot afford licensed services may qualify for subsidy. Some governments subsidize the entire cost of child care. Others set daily maximum rates for their subsidies. Eligible families may not receive the service, however, because there are simply not enough licensed spaces. Parents who cannot find a licensed space or who cannot pay the difference between the actual cost of care and the subsidy must rely on unlicensed child care provided by friends, babysitters, neighbours, or nannies.⁴⁴

Unlicensed child care means the care is not regulated by government standards. Family day-care homes may be licensed or unlicensed depending upon the preferences of the caregiver. Governments set limits on the number of children who may be cared for in a private home.

Funding arrangements for licensed child care vary by jurisdiction. As indicated, some governments offset the high cost of licensed child care through subsidies for parents whose net incomes fall below certain levels and/or through grants to not-for-profit centres. The federal government contributes to the cost of child care under CAP. It pays for child care subsidies to parents enrolled in training courses sponsored by the Department of Employment and Immigration and for child care on Indian

reserves. It also provides indirect tax assistance to offset costs through the

child care expense deduction.

A link between NRTs and the need for child care clearly exists — in theory at least. An absolute increase in numbers of children will create a demand for child care services. Yet the link may not be as direct as it appears.

The costs of licensed child care might be too high for many families, especially if they have several preschool children as a result of successful NRT procedures. While families may qualify for subsidy, there may not be enough licensed spaces for them to take advantage of this assistance. They may have to make informal arrangements with a babysitter or relative.

In short, the actual demand for child care services may not increase dramatically as a result of NRTs. However, the latent demand may be high. If licensed child care were more affordable through increased government subsidies to parents and/or services, then many more families might seek this care.

Services for Children with Special Needs

It is impossible to predict the extent to which NRTs will generate a demand for services for children with special needs. In some cases, increased use of PND to screen for genetic problems and fetal surgery may reduce the need for these services. Some parents may decide, upon learning of a serious condition, to end the pregnancy. In other cases, fetal

surgery may be able to correct a diagnosed anomaly.

If the use of NRTs becomes more widespread, there may be a greater demand for early intervention services. Certain NRT procedures, such as IVF, often are associated with multiple births. A British survey found that 55 percent of mothers of quadruplets and higher-order births and 31 percent of mothers of triplets had undergone some treatment for infertility. By contrast, only 7 percent of mothers of twins and 3 percent of mothers of single babies had undergone such treatment. The authors concluded that "drugs and procedures for infertility, including assisted induction of ovulation, contributed substantially to the numbers of triplet and higher order births in our study."

Multiple births are, in turn, frequently associated with low birthweight. The above study found that most triplets or higher-order babies were of low birthweight (less than 1 999 grams). Fewer than six percent of single babies weighed less than 2 500 grams at birth compared with almost one-half of twins, more than 90 percent of triplets, and virtually all of the

quadruplets.46

The results of the study, while tentative, found that the triplets and higher-order births developed quite normally in some areas but showed a higher prevalence of problems, including cerebral palsy and congenital malformation.⁴⁷

While low birthweight babies may be at higher risk of certain developmental delays or learning disabilities, some recent Canadian data

indicate that the potential effects of low birthweight can be mitigated through early intervention. With proper intervention at the early post-natal stages, the need for various forms of long-term services may be reduced, if not eliminated, for many children.

A study undertaken by McGill University and Montreal's Jewish General Hospital compared the development of 100 children of low birthweight with that of 100 children of normal birthweight. Some children were assessed at age six, while others were assessed at age nine.

The results showed that, on average, the low birthweight babies fared as well as the normal birthweight babies on a wide range of scores, including intelligence quotient, motor/visual skills, and academic skills. Some low birthweight children scored lower than normal on all measures and were seriously delayed in their development. On the whole, however, the results indicated that extreme prematurity in neurologically intact children did not in itself adversely affect cognitive development. While a certain number of very low birthweight babies will require more intensive, long-term follow-up, it is impossible to identify these children at birth.

The following section describes the social services and income support programs available to assist families caring for children with special needs. Ultimately, the more widespread use of PND and fetal surgery may reduce the need for such services if parents decide not to proceed with the pregnancy.

Early Intervention Services

Early intervention refers to a variety of services designed to assist infants and preschool children with special needs, such as developmental delays in motor, language, cognitive, or sensory skills. These incorporate both health-related and social services that include but are not limited to physiotherapy, audiology, speech therapy, parent-child play sessions, preschool programs such as "head start," and parent education programs.

The Home Services Program in Newfoundland, for example, offers home-based training for parents of children with developmental delays. The Early Childhood Intervention Program in Nova Scotia provides home-based training and support to parents of children with developmental disabilities from birth to age five. These programs are supported by the social services ministries in both provinces.

Funding arrangements vary throughout the country. Early intervention services delivered in hospital and health care settings are supported largely through health dollars. Services primarily social in nature are funded largely through welfare dollars. School-based programs are funded through provincial and territorial revenues directed toward education.

Income Assistance

Income assistance for special needs is provided through direct cash transfers and indirect tax assistance. The following provinces grant cash assistance to help families with severely disabled children: Newfoundland

(Special Child Welfare Allowance); Prince Edward Island (Family Support Service); Nova Scotia (In-Home Support Program); Quebec (Allowance for Handicapped Children); and Ontario (Handicapped Children's Benefit).

Under the In-Home Support Program in Nova Scotia, for example, a monthly maximum cash benefit of \$300 is provided to offset disabilityrelated costs, such as medication, transportation, and respite. The amount varies by family income and need. Quebec provides a non-taxable, flat-rate monthly Allowance for Handicapped Children. The amount was \$116.88 in January 1992. Beneficiaries must qualify on the basis of medical certification.

Recognition of extra costs through the tax system is another form of assistance. The federal government provides indirect assistance to offset disability-related costs through the disability credit, worth \$700 in 1992, and the medical expenses credit, worth 17 percent of allowable medical expenses in excess of three percent of net income in 1992. disability-related items are exempt from provincial sales tax.

Support to Families

Several provinces provide goods and services to families caring for children with severe disabilities. Under the Handicapped Children's Service Program in Alberta, for example, parents receive full or partial reimbursement for expenditures arising from the disabling condition. Funds may be provided to cover the costs of a special service, such as a day program, medication, transportation, and respite care. Equipment such as wheelchairs, hearing aids, and prosthetic appliances is available through the Alberta Aids to Daily Living Program.

Another example of a relatively comprehensive package of services is the At Home Program in British Columbia. Eligible families may qualify for a variety of goods and services, including health care, medical equipment and maintenance/repair costs, drug coverage, dental care, hearing aids,

and respite care.

Most provincial and territorial governments provide varying combinations of services, including home care, respite, and additional funds for child care centres. However, the special needs of some children may be so extreme that community-based services are unable to meet these needs. These children often are placed outside the family home in a residential arrangement that includes health-related and social services.

Residences intended solely for children are funded under CAP. Residences for older persons are supported through an extended health care services arrangement with funds from CAP and EPF. There is currently a strong movement, supported by official federal policy, toward

the closure of institutions.

Services That Substitute for Family Care

Child Protection Services

Parents have primary responsibility for meeting their children's physical, intellectual, emotional, and social needs. Yet some parents may be unable to carry out their parenting role as a result of death, divorce, imprisonment, prolonged hospitalization, or extreme stress.

Child protection services are designed to protect and care for children who are victims or suspected victims of abuse or neglect, or who are temporarily without parental care. Protection services are delivered by child welfare agencies, which derive their mandate from provincial or territorial law.

Formerly, protection took the form of removing children from their natural homes. Today, there is a trend toward keeping families intact through counselling, providing services that supplement family care, and removing the abuser. When these options are inappropriate or fail to protect the child, parental care may be substituted with other forms of care described below.

Services that substitute for parental care are mandated and regulated by provincial and territorial law. Despite the differences in definitions and service delivery, all the regulatory acts list the factors to consider in determining whether a child needs protection. The services that substitute for parental care include foster care, group care, and adoption.⁴⁹

Foster care provides substitute care for a temporary or extended period during which a child's family cannot care for him or her. Children with severe emotional, mental, or physical problems may be placed in a group or foster home that cares for four to eight children. Depending on the severity of their needs and the available resources, they may be placed in a residential setting. These facilities generally provide some form of treatment by professional staff, such as psychologists or social workers.

Adoption represents permanent alternative care. Provincial adoption laws are relatively congruent, thereby facilitating interprovincial adoption. The various provincial and territorial acts establish the mechanisms for changing guardianship. Several provinces permit private adoptions for persons who wish to adopt children through organizations other than the designated child welfare agency.

An important trend in adoption is likely to have implications for NRTs. Over the past decade, there has been a significant increase in the number of adopted children seeking information about themselves and their parents. Several agencies have opened or expanded adoption and reunion registries. Judging from the interest that adopted children have expressed in their birth parents, children conceived through NRTs probably will have a similar interest in information about their biological parents. This raises questions about whether and how this information should be made

available and the need for counselling for persons concerned about their

biological parentage.

As noted in Part 1, adoption represents an option for childless couples. But the number of children available for adoption has declined substantially as a result of several factors, including trends in child welfare toward maintaining children in their natural homes.

The extent to which families that conceive children through NRTs will require child welfare services is unknown. In some cases, these families may experience physical, emotional, and financial stresses that make them more vulnerable to abusing their children. In other cases, parents may be so happy about the birth that they may be at lower risk than the general population of neglecting or abusing their children. The third possibility is that these families resemble the rest of the population, and only a small percentage of families may require intervention by child welfare authorities.

Conclusions

The Relevance of Social Welfare to NRTs

This paper considered the aspects of the social welfare system that relate to use of NRTs. The social welfare system seeks to redistribute social benefits to reduce inequalities. Through selected pieces of legislation and funding arrangements, the social welfare system essentially determines access to NRTs.

More specifically, the definition of certain health care services as "medically necessary" under the Canada Health Act determines whether the costs of these services will be covered through provincial and territorial health plans. Currently, NRTs are defined as medically necessary only in Ontario — the one jurisdiction that covers the costs as an insured health care service — with obvious implications for access to these technologies.

The social welfare system has an impact upon general well-being and, by implication, upon reproductive health. Certain social services are directly involved in reproductive health through sexuality education and work with street youth. These programs are intended to curb the spread of sexually transmitted diseases. They may affect the long-term demand for NRTs by reducing the incidence of infertility linked to these diseases.

The availability of certain social services might have a direct impact upon the demand for NRTs. For example, adoption services influence this demand because infertile couples often choose to adopt children. The number of children available through adoption, however, has fallen dramatically over the past decade. The availability of child care services may influence childbearing decisions.

NRTs may create demands or pressures upon the social welfare system. More specifically, NRTs may have a potential impact upon services

that support families, services that supplement family care, and services that substitute for family care.

In the area of services that support families, there likely will be a greater need for counselling as a result of NRTs, given the stresses associated with these procedures. The demand will arise in response to problems of infertility, fetal anomalies identified through PND, and stressful procedures associated with some NRTs. If NRT procedures are successful, there may be an increased need for counselling and support during prenatal, perinatal, and post-natal care.

NRTs also may generate a long-term counselling need. Couples may experience marital stress arising from physical exhaustion and financial strain if they experience multiple birth. Individuals confused by or concerned about their parentage may seek assistance.

There may be a need for early intervention services to mitigate the effect of developmental delay which arises from multiple birth, often associated with low birthweight. The need for special services over time is unpredictable, however, given contradictory research findings concerning the long-term impact of low birthweight upon development. In addition, the demand for services for children with special needs may decrease as a result of the more widespread use of PND and fetal surgery.

The impact of NRTs upon income programs will vary. More children may generate higher costs for the Child Tax Benefit. The actual extent to which higher costs will be generated through these programs depends upon level of income.

The demand for income assistance to offset the costs associated with multiple birth, child-rearing, and child care will depend upon each family's unique financial circumstances. Thus, it is impossible to predict the extent to which families seeking NRTs will require financial assistance from programs such as welfare.

There likely will be pressures for certain services that supplement family care, particularly homemaker assistance and child care. In fact, the need for supplemental services may be high for families with multiple births because of their need for extra help and respite.

Demand for these services cannot be predicted. The need for supplemental care is a function of access to informal supports as well as income level. Some families may not require supplemental services because they have extra assistance (e.g., grandparents, friends).

High-income families may decide to purchase these services on their own (e.g., housekeeper, nanny) without apparent burden to the social welfare system. In fact, only higher-income families now may be in a position to seek NRTs because of associated user fees. Unless access is opened through insured health coverage in all jurisdictions, the group of users may be confined to a relatively higher-income band — a group that likely would be in a position to purchase supports, such as homemaker assistance and child care.

Finally, services that substitute for family care protect children in the event of abuse or neglect. It is impossible to conclude that there will be greater demand for these services as a result of NRTs. Uncertainty arises from two contradictory factors.

In some cases, the financial strains and physical exhaustion associated with multiple birth may create the conditions for child abuse. At the same time, families that have had successful NRT outcomes may feel so positively about the birth that they are unlikely to neglect or abuse their children. Consequently, they may have less need for these services than the general population.

In the absence of solid research data, it is difficult to identify the impact of NRTs upon social welfare. Nonetheless, it is possible to infer the need for services such as counselling, early intervention, homemaker assistance, and child care by virtue of the psychological, physical, and financial stresses that some couples may experience in relation to NRTs.

Finally, the impact scenario must be placed within context. The number of children born through assisted conception procedures is relatively small. Even though NRTs are likely to place demands upon some components of the social welfare system, the net impact will be minor in cost terms. The social welfare system will not suddenly be overwhelmed with the problems of enormous numbers of families that conceive children through NRTs. The real impact may be more qualitative; certain components of the social welfare system, such as counselling services, may need to respond to new problems (e.g., making decisions on the basis of PND).

Implications for the Commission

This study confirms that the social welfare system has an important influence upon the demand for NRTs. In turn, NRTs have created and will continue to create demands upon the social welfare system. There are significant areas of interface between the fields.

In formulating its recommendations, the Commission may wish to address the following:

- 1. the issue of whether NRTs are a social or medical necessity and the funding and accessibility issues arising from this determination:
- 2. the need to ensure social conditions, such as adequate incomes, decent affordable housing, health care services, and education, that promote general well-being and, by implication, reproductive health:
- 3. the need for more preventive programs focussed upon promoting reproductive health and curtailing the spread of sexually transmitted diseases;

- 4. the problems in the current adoption system, raising questions about international adoption procedures and the social acceptability of childlessness;
- 5. a likely increase in the demand for counselling services associated with all stages of NRTs: diagnosis of infertility; various phases of reproductive protocol; PND; prenatal, perinatal, and post-natal care; the long-term psychological impact upon children; and marital impact;
- 6. the fact that there are no standards for counselling in these specialized areas;
- 7. the need for early intervention services to mitigate developmental delays associated with low birthweight;
- 8. the possible rise in the costs of selected income programs, notably the Child Tax Benefit and child care expense deduction:
- 9. the possible increased need for homemaker assistance and child care services, depending upon access to informal supports and income level:
- 10. a potential increase in the need for programs and services such as social assistance (welfare) and child protection.

The federal government can assume a leadership role in relation to social welfare and NRTs in three areas: prevention of infertility, availability of services, and research and training. With respect to prevention, the federal government can ensure the social conditions that protect health in general and reproductive health in particular. It can provide unequivocal support to programs that promote adolescent reproductive health.

In the area of services, the federal government can offset some of the financial strains of NRTs through direct income programs and indirect transfers via the tax system. Its intervention with respect to social services is much less direct. However, it can take immediate action to halt the erosion of services, which it has helped create through successive cuts to federal transfers for health care and the capping of CAP. These federal actions make it almost impossible to maintain existing levels of service, let alone respond to new demands, such as the increased need for counselling services likely to arise as a result of NRTs.

Finally, the federal government can build the knowledge base in this field by promoting research on the prevention of infertility as well as the developmental, psychological, social, and financial impact of NRTs. It can encourage high quality practice through developing training modules that identify the core areas of knowledge and skill required for counselling in the field of PND and NRTs. There is precedence for this type of federal involvement in other areas of human need, including child sexual abuse, self-help, and the prevention of drug abuse.

Appendix: Overview of Social Welfare

Historical Base

Social welfare has its roots in the industrial revolution of the nineteenth and twentieth centuries. The transition from an agrarian society created an uncertain economic environment. The new system of industrial wages left workers particularly vulnerable during illness, unemployment, and old age. Traditional social institutions, such as the family and community, were unable to cope with long periods of lost income as well as problems associated with industrialization and urbanization.

It was clear that these traditional institutions would require broad extra assistance and support which only the state was in a position to provide. Indeed, social welfare is based on the assumption that the state recognizes the need and desirability of providing goods and services through programs such as child benefits and Old Age Security pensions

that fall outside the wage employment structure.

One of the most serious problems arising from industrialization was its impact upon children: the exploitation of children in factories and the plight of neglected, abused, and delinquent children. In 1887, the Toronto Humane Society was founded to protect children (and animals) from cruelty. To provide proper protection for children, the Society soon realized that it required authority to act. It pressured the Ontario legislature to pass an act for the protection of children in 1888. In 1893, a more advanced piece of legislation was introduced that emphasized public responsibility through the appointment of a superintendent of neglected and dependent children.⁵¹

The act was a milestone — a precedent for child welfare legislation and a model for other provinces. It also provided public funds for the provision of services. Before the 1900s, voluntary and religious organizations had played the major role in service provision. In fact, the roots of social

services can be found in charitable and religious movements.

As the economy developed at the end of World War I, and as the population settled into urban areas, the federal and provincial governments began to establish the welfare state. Much early activity was concerned with ensuring stable, secure incomes in an increasingly uncertain economic environment. Quebec introduced the Workmen's Compensation Act of 1909, which established a system of compensation for various degrees of disability. The Ontario Workmen's Compensation Act of 1914 provided compulsory income protection against major risks to the continuity of income in an industrial society: work-related illness, disability, or death.

In addition to ushering in an industrial environment, World War I had a profound impact upon Canada's socioeconomic structures. The pervasive influence of governments throughout the war provided a sense of the role that they could play in the lives of Canadians. To manage the economy, the federal government imposed a tax on personal income.

Governments also were called upon to play a major role in providing financial support for wounded soldiers, widows, and orphaned children. The post-war mothers' pension movement evolved partly in response to the increased numbers of widows with small children. The growth of one-parent families was the result of family breakup, fuelled by the shift from tightly knit rural communities to anonymous urban areas. One of the first pieces of legislation to support single parents was the Mothers' Pension Act of British Columbia of 1920.

The Depression brought massive unemployment and financial hardship for many Canadians. Close to 15 percent of the population received some form of public relief. Throughout the 1930s, most relief was provided by local parishes and municipal governments. When the numbers became too large for local governments to handle, there was increasing pressure for federal involvement. In 1940, the federal government passed the Unemployment Insurance Act.

Ottawa had been slow to respond to the problem for two reasons. First, a constitutional amendment was required because this involvement fell outside the federal domain. Second, the federal government preferred to act in a "residual" mode. In fact, residualism dominated the social welfare field until the 1940s.

Philosophical Base

The "residual" mode of social welfare refers to a minimalist response in which assistance is provided to persons in need only after all other avenues have been explored. The private market and family act as the key sources of support, after which governments intervene as a last resort. Residual services, such as welfare and child protection, have evolved in response to inadequacies of the market economy or problems in the family. ⁵²

The widespread impact of the Depression promoted a shift to the institutional concept of welfare. This concept recognizes that life in a predominantly urban, industrialized world creates risks to income security and social well-being. Governments can help minimize these risks and

provide the social supports required to function successfully.

The institutional notion helped shape many social welfare programs, such as family allowances and medicare, introduced after World War II. However, there has been and remains a tension between supporters of residual and institutional concepts of social welfare. The latter approach is generally considered to be an intrusion in the private market — the primary mechanism for distributing income, goods, and services in the Western world.

The tension was illustrated by the debate about universal and targeted approaches to child benefits. Some favoured a universal approach to family allowances because these were deemed to represent collective social interest in family well-being. They opposed more targeted benefits, which

may provide more generous assistance, because targetting shifts the system such that only those in need would be eligible for aid. The benefit would become last resort assistance rather than a measure that promotes general well-being.

Cost-Shared Programs

Canada Assistance Plan

The Canada Assistance Plan (CAP) is the major piece of federal legislation under which welfare and social services are supported. Introduced in 1966, CAP replaced several pieces of legislation directed toward specific groups, such as elderly persons or single-parent mothers.

Under CAP, the federal government shares with the provinces and territories in 50 percent of the costs of welfare and social services for Canadians with low or modest incomes. Costs may be shared under CAP's assistance or welfare services provisions.

Under the assistance provisions, the federal government shares in the costs of welfare or services provided to persons in need. The assistance provisions allow for sharing the costs of basic requirements, special needs, and prescribed services. Basic requirements are defined as food, shelter, clothing, fuel, utilities, household supplies, and other personal items. Because there are no federal guidelines for amounts that should be provided for basic needs, actual assistance varies throughout the country.

CAP also shares in the cost of special items or services required for the safety, well-being, or rehabilitation of persons in need. Many health-related goods and services, such as medication, dietary supplements, and special equipment, are funded through these provisions.

Finally, costs may be shared for prescribed services defined under CAP legislation as rehabilitation, counselling and assessment, homemaker assistance, and day-care. To qualify for federal cost-sharing, these services must be purchased on behalf of a person in need. The individual need not be a welfare recipient to be eligible for a prescribed welfare service.

The key criterion for sharing under the assistance provisions is that the costs must be incurred on behalf of individuals or families in need—that is, they must qualify for assistance on the basis of a needs test. While needs tests vary by jurisdiction, they generally work in the following way.

Ae needs test takes into account the household's basic needs (e.g., food, clothing, shelter) and special needs (e.g., medications, special diets). The resources available to meet the household's needs are then determined; these include income from employment, pensions, and government transfers. Certain sources of income are considered exempt in the calculation of income.

The household is deemed to qualify for assistance when it has a "budget deficit" — i.e., its needs exceed available resources. In addition, the household cannot have cash or liquid assets that exceed certain levels.

Cost-sharing is also permitted under CAP's welfare services provisions. In this case, funds cannot be transferred directly to individuals or families. The welfare services provisions allow the flow of funds to services only.

Welfare services are designed to lessen, remove, or prevent poverty, child neglect, or dependence on public assistance. They include rehabilitation; counselling, assessment, and referral; homemaker assistance; day-care; consulting, research, and evaluation services with respect to welfare services; and administrative, secretarial, and clerical services. Welfare services do not include services related primarily to corrections, health care (with the exception of certain health-related items funded as special assistance), hospital or school social services, and mental health services.

Costs are shared with provinces and territories for services provided to persons in need (as described) or to persons likely to be in need. Individuals and households generally are considered likely to be in need if their net income falls below certain levels. According to the federal guidelines, persons or families likely to be in need must qualify on the basis of a provincial/territorial income test or must be recipients of the federal Guaranteed Income Supplement for seniors, which itself requires an income test for qualification.

In contrast to needs testing, which takes into account needs, resources, and assets, an income test looks strictly at level of income. While provinces and territories set their own income tests, the federal government sets the guidelines for levels of net income that qualify for cost-sharing. Households with net incomes up to certain levels are eligible for a full subsidy. Beyond that point, families may be eligible for a partial subsidy until their net income reaches the cut-off point. They are no longer eligible for assistance under CAP once their net income exceeds the cut-off point.

The welfare services provisions also allow for costs to be shared for certain target groups designated as a "community of need." Needs and income tests can be replaced by proxy indicators. For example, services may be provided to residents of a public housing project. Prospective service recipients automatically qualify by virtue of their residence.

One of the major differences in funding under CAP's assistance and welfare services provisions is that services are eligible for cost-sharing under the latter provisions if they are delivered by a provincially approved agency. Under the welfare services provisions, funds cannot be directed toward commercial agencies. The latter can only be publicly supported through fee-for-service reimbursement under CAP's assistance provisions. CAP also shares in the cost of extended health care services delivered in residential settings on behalf of persons in need.

In 1989-90, the federal government transferred \$4.9 billion to the provinces and territories under CAP.⁵³ The federal government estimates its 1990-91 transfers as almost \$5.3 billion.⁵⁴ In a move to reduce the deficit, Ottawa announced it would limit increases in CAP payments to

Ontario, Alberta, and British Columbia to five percent a year from the 1990-91 fiscal year until the end of 1994-95. The restraint was part of a larger package of measures introduced under the federal government Expenditures Restraint Act that included cuts in federal transfers for health care and post-secondary education.

British Columbia challenged the proposed policy in the provincial Court of Appeal, arguing that it had a legitimate expectation that the federal government would not change its commitment without provincial consent. The Court ruled unanimously in favour of the province. The judgment was challenged by the federal government in the Supreme Court of Canada. In a unanimous decision rendered in August 1991, the Supreme Court defended the prerogative of the federal government to limit spending in this way.

Established Programs Financing

Health care services are regulated under the Canada Health Act of 1984, which replaced the Hospital Insurance and Diagnostic Services and the Medical Care acts. The Canada Health Act establishes the criteria that must be in place before federal financial contributions to health care are made.

Two types of health care are defined in the act. *Insured health care*, or what is generally called *medicare*, refers to medically necessary hospital services, medically required physicians' services, and surgical or dental services that require a hospital for their proper performance. *Extended health care* refers to services made available in out-patient settings, in facilities such as nursing homes, and in private homes in the form of home health care.

The Canada Health Act sets out five criteria that provinces and territories must meet to receive federal health care funding. These criteria are comprehensiveness, universality, public administration, portability, and accessibility.

Comprehensiveness means the costs of services provided by hospitals and medical practitioners are covered by provincial or territorial health care plans. Universality means all residents of a province or territory are eligible for insured health care services. Public administration requires the insured services to be delivered by a public authority on a non-profit basis. Portability ensures that Canadians moving from one province or territory to another are covered by medicare. Accessibility means insured health care services must be available without impediments such as user fees.

These five criteria apply only to insured health care services, not extended health care services. This distinction is important: it explains why provinces and territories can charge fees for health-related services that are not defined as medically necessary.

The purpose of the act is to control quality by setting national standards. The funding of health care services falls under a different act administered by the federal Department of Finance. Formerly, it was called

the Federal-Provincial Fiscal Arrangements and Established Programs Financing Act — hence the continued reference to the EPF arrangement. Transfers now are made under the Federal-Provincial Fiscal Arrangements and Federal Post-Secondary Education and Health Contributions Act.

Under this act, provinces and territories are entitled to equal per capita federal health contributions indexed annually to increases in the Gross National Product (GNP). The total federal contribution is based on the 1975-76 national average per capita costs escalated by population and GNP growth to a current value.

In 1977-78, the federal government reduced its income tax rates so that the provinces could raise theirs, at no cost to taxpayers. The current value of this tax transfer is deducted from the total estimated entitlement and the remainder is paid in cash. To ensure that the poorer provinces have the same capacity to pay for health and post-secondary education as the richer provinces, the value of the tax transfers was equalized. The total federal per capita entitlement is the same throughout the country. In addition to cash and tax transfers, the federal government provides an equal per capita grant to provinces and territories to help pay the costs of extended health care services.

The EPF arrangement has been the subject of considerable debate and much acrimony between Ottawa and the provincial/territorial governments. As a deficit cutting measure, the federal government announced in its 1986 budget that EPF transfers no longer would follow GNP growth but would be tied to GNP minus two percentage points.

In 1989, Ottawa indicated it would subtract yet another percentage point from the indexation formula. In the 1990 budget, it announced that EPF transfers would be subject to a two-year freeze, followed by a formula of GNP minus three percentage points beginning in 1992-93. In the 1991 budget, the Finance Minister extended the freeze on per capita EPF entitlements to 1994-95. As of 1995-96, growth in EPF entitlements will be limited to a rate of growth of GNP per capita minus three percentage points.

In 1989-90, the federal government transferred nearly \$5.3 billion to the provinces and territories in respect of insured health care services. Projections show that the new formula will reduce federal transfers to the point where these will soon end. Cash payments to Quebec, for example, will disappear by 1996-97. Cash payments to Ontario will end by 2002-2003. By 2009-2010, all federal EPF transfers will disappear. 56

Federal changes to the transfer formula will have a serious impact upon health care. First, a significant amount of money is being withdrawn from the health care system. Provinces and territories will need to respond by cutting services, raising taxes to offset the federal reductions, or redefining certain services as no longer medically necessary to introduce user fees.

Second, the federal government can do little if provinces and territories violate the criteria set out in the Canada Health ${\rm Act-e.g.}$, violate the

accessibility criterion through the imposition of user fees. Ottawa will be less able to enforce standards by threatening to withhold funds. There will be no contribution to hold back, or the amount will be so minimal that provinces and territories will not be afraid to lose it, especially if the loss can be more than offset by user fees.

Notes

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- 16. Report on Adolescent Reproductive Health, 31.
- 17. Ibid., 33.
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- 19. J. Harris and J. Melichercik, "Age and Stage-Related Programs," in *Canadian Social Welfare*, 2d ed., ed. J.C. Turner and F.J. Turner (Don Mills: Collier Macmillan Canada, 1986), 169.
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- 24. Ibid., 164.
- 25. Canada, Status of Women Canada, Report of the Task Force on Child Care (Ottawa: Minister of Supply and Services Canada, 1986), 6.
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Mandate

(approved by Her Excellency the Governor General on the 25th day of October, 1989)

The Committee of the Privy Council, on the recommendation of the Prime Minister, advise that a Commission do issue under Part I of the Inquiries Act and under the Great Seal of Canada appointing The Royal Commission on New Reproductive Technologies to inquire into and report on current and potential medical and scientific developments related to new reproductive technologies, considering in particular their social, ethical, health, research, legal and economic implications and the public interest, recommending what policies and safeguards should be applied, and examining in particular,

- (a) implications of new reproductive technologies for women's reproductive health and well-being;
- (b) the causes, treatment and prevention of male and female infertility;
- (c) reversals of sterilization procedures, artificial insemination, in vitro fertilization, embryo transfers, prenatal screening and diagnostic techniques, genetic manipulation and therapeutic interventions to correct genetic anomalies, sex selection techniques, embryo experimentation and fetal tissue transplants;
- social and legal arrangements, such as surrogate childbearing, judicial interventions during gestation and birth, and "ownership" of ova, sperm, embryos and fetal tissue;
- (e) the status and rights of people using or contributing to reproductive services, such as access to procedures, "rights" to parenthood, informed consent, status of gamete donors and confidentiality, and the impact of these services on all concerned parties, particularly the children; and
- (f) the economic ramifications of these technologies, such as the commercial marketing of ova, sperm and embryos, the application of patent law, and the funding of research and procedures including infertility treatment.

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